

The American Journal of **DIGESTIVE DISEASES**

An Independent Publication

DEVOTED TO GASTRO-ENTEROLOGY AND NUTRITION

ORIGINAL CONTRIBUTIONS

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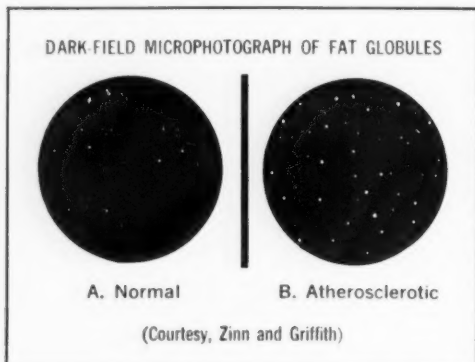
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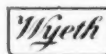
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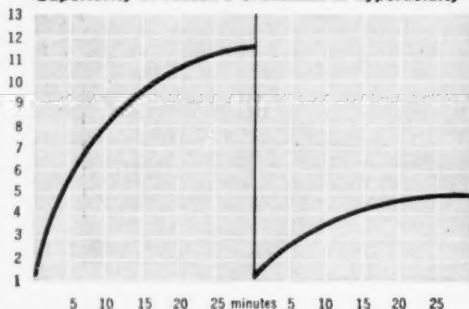
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CHRONIC SUPERFICIAL GASTRITIS: OBSERVATIONS ON CLINICAL AND HISTOPATHOLOGIC SIGNIFICANCE

EDDY D. PALMER, LT. COL., M. C., Washington, D. C.

CHRONIC superficial gastritis is one of the three common chronic gastritides encountered by the gastroscopist. It presents a striking endoscopic picture and has been generally accepted as a significant clinical disease. Schindler's (1) monograph should be consulted.

Among the last 2500 patients examined gastroscopically at this hospital, 83 received the diagnosis of chronic superficial gastritis. It is the purpose of this communication briefly to review local clinical experiences with the disease, to discuss the gastroscopic picture, and to present the results of mucosal biopsy studies.

PATIENT COMPOSITION

The gastroscopic diagnoses were made during the search for an explanation for upper gastrointestinal symptoms. The 83 patients included only three females and one Negro, although approximately 15 percent of the Gastroscopic Clinic's population are women and 20 percent are Negroes. The number of patients per age-decade from the second through the seventh decades was, respectively, 6, 27, 29, 9, 9, and 3.

Although the postoperative stomach frequently shows a type of gastritis which appears similar to chronic superficial gastritis gastroscopically, previous histologic studies have shown this to have special mi-

TABLE I

OTHER SIGNIFICANT DISEASES FOUND AMONG THE 62 PATIENTS WHOSE SUPERFICIAL GASTRITIS WAS NOT CONSIDERED THE BASIS FOR ILLNESS

Diagnosis	No. instances
Duodenal ulcer	22
Gastric ulcer	9
Virus hepatitis	9
Anxiety reaction	8
Hiatus hernia	8
Cholelithiasis	5
Carcinoma of stomach	4
Laennec's cirrhosis	3
Mallory-Weiss syndrome	2
Hypochondriasis	2
Carcinoma of pancreas	2
Cholecystitis	2
Pregnancy	1
Acute pharyngitis	1
Schistosomiasis	1
Sarcoma of stomach	1

From the Gastrointestinal Section, Walter Reed Army Hospital, Washington, D. C.

Submitted May 25, 1953.

croscopic features of its own. For this reason, none of the patients included here had had any gastric surgery.

CLINICAL OBSERVATIONS

After thorough clinical investigation, it was concluded that demonstrated disease other than the gastritis had been responsible for the illnesses of 62 patients. Altogether 80 other important upper gastrointestinal or more generalized diseases were diagnosed (table 1).

Final clinical evaluation indicated that chronic superficial gastritis had been responsible for the illness

TABLE II

CATEGORIZATION OF THE SYMPTOM COMPLEXES OF THE 21 PATIENTS WHOSE GASTRITIS WAS CONSIDERED TO BE THE CAUSE OF ILLNESS

Symptom complex	No. patients
Burning epigastric pain, relieved by food	9
Sudden hematemesis the first and only symptom	3
Gas, pressure, epigastric fullness	3
Complex dyspepsia	2
Periodic epigastric cramps	2
Postprandial nausea and vomiting	2

of 21 patients. The subjective pictures of these cases are categorized in table 2, and the duration of symptoms in table 3.

TABLE III

DURATION OF SYMPTOMS: 21 PATIENTS WHOSE GASTRITIS WAS CONSIDERED TO BE THE CAUSE OF ILLNESS

Duration	No. patients
1 - 2 weeks	2
3 weeks	1
5 - 8 weeks	4
9 - 12 weeks	3
21 - 29 weeks	2
40 - 45 weeks	2
1 - 2 years	3
3 years	1
5 years	2
7 years	1

Sixteen of the 83 patients had had significant upper gastrointestinal hemorrhages. In nine no possible source other than chronic superficial gastritis was found. More

important, in 11 instances gastroscopic examination carried out during active hemorrhage following ice-water lavage showed that the bleeding was originating from multiple gastric erosions. The only subjective evidence of illness in three patients was the hemorrhage.

GASTRIC SECRETORY ACTIVITY

Histamine-stimulated gastric analyses were made in 27 instances (table 4). The results showed all degrees of free-acid secretion, without any general abnormal tendency.

TABLE IV
RESULTS OF GASTRIC ANALYSES:
MAXIMUM FREE-ACID RESPONSE TO HISTAMINE

Maximum free acid: mEq/l	No. patients
0	3
1 - 10	3
11 - 20	2
21 - 30	6
31 - 40	2
41 - 50	3
51 - 60	5
75	1
83	1
99	1

GASTROSCOPIC APPEARANCES

The disease as observed gastroscopically was a generalized one in most cases. It was found that all of the gastric mucosa was involved in 50 percent of the patients, and that more than half was involved in 90 percent. One of the two constant findings was mucous exudate, a mixed thick and thin opaque gray material without bubbles, occurring in small amounts either applied to the mucosal surfaces as heavy plaques or running between the rugae. When examined microscopically, it was found to consist of pus cells, mucus, and exfoliated surface epithelium cells. All cases also showed small patches of mucosal hyperemia—rarely large diffuse areas and never generalized hyperemia. Erosions were present in one-third of the cases. Edema was apparent in only five.

Patchy chronic atrophic gastritis was dispersed through the superficial process in eight instances.

RESULTS OF SERIAL EXAMINATIONS

The opportunity to follow the gastroscopic changes by serial examination was taken in 19 cases, and 54 examinations were made of the group. On the basis of general appearances, such as the amount of purulent exudate and intensity of hyperemia, it has been the custom on this Section to categorize the severity of chronic superficial gastritis as "severe," "moderate," and "mild." The relative changes found upon serial gastroscopic examinations are outlined in table 5. All patients were under hospital treatment during at least a

TABLE V
EVALUATION OF THE SEVERITY OF CHRONIC
SUPERFICIAL GASTRITIS UPON SERIAL EX-
AMINATIONS, WITH INTERVALS BETWEEN
EXAMINATIONS (WEEKS): 19 PATIENTS

1st exam.	Weeks	2nd exam.	Weeks	3rd exam.	Weeks	4th exam.	Weeks	5th exam.
Mild	4	mod	3	norm	1	mild	3	mild
Mod	1	mod	1	norm	5	norm	5	norm
Mod	2	mild	3	mod	3	norm	250	atrophy
Sev	2	sev	5	norm	6	norm		
Norm	2	mild	2	mild	13	mild		
Sev	6	sev	3	sev				
Norm	38	sev	5	norm				
Mod	1	mod	1	mod				
Mod	8	norm						
Mod	1	mod						
Mod	3	mild						
Sev	4	mod						
Sev	3	mild						
Mild	1	mild						
Norm	12	mod						
Mild	2	norm						
Mod	2	norm						
Sev	14	sev						
Sev	1	sev						

part of the observation period. In general, it was found that the apparent severity of the disease could change appreciably in the course of a week, but that in most instances a month or more was required. The disease in some cases remained static over long periods. In some patients the end result was a normal mucosa; in others the process disappeared, only to recur at a later date.

The development of chronic atrophic gastritis was observed in one patient. This progression of events has previously been witnessed in other patients. The present case was followed for five years, and, even though the initial series of examinations had shown a return to mucosal normalcy on hospital treatment, he eventually returned with generalized atrophic gastritis.

TREATMENT

Without particularly good rationale, it has been the custom on this Section to treat chronic superficial gastritis by a moderate ulcer regimen: bland diet, belladonna, antacids, and interdiction of tobacco. The regimen has usually been continued several months, if at all practicable. Gastroscopic evidence frequently indicated improvement or clearing of the mucosal disease (table 5).

Subjectively, however, the results of treatment were

very difficult to evaluate. The multiplicity of abdominal and general diagnoses was, of course, the reason. The general impression was that a regimen as prescribed for ulcer has been worthwhile.

HISTOLOGIC STUDIES

Biopsies of the diseased gastric mucosa were taken by vacuum-tube technic in 13 instances. The specimens were removed from the anterior wall of the pars media, close to the greater curvature, approximately in a line with the axis of the esophagus. Histopathologic correlations were good, but the gastroscopic categorization of gastritis severity was not necessarily reflected in the severity of microscopic change. Two of the 13 biopsy specimens were entirely normal, as normalcy has previously been defined (2). There was one instance of chronic atrophic gastritis, and 10 which were considered to demonstrate the histopathologic picture of chronic superficial gastritis. The findings among the 11 abnormal specimens are described here.

The thickness of the various mucosal layers, as measured on fixed sections, was normal in the 10 pertinent specimens (table 6). The muscularis mucosae was normal in all, without cellular infiltration, muscle fragmentation, or hyperplasia.

TABLE VI
THICKNESS OF MUCOSAL LAYERS (mm.),
AS COMPARED WITH NORMALS (2)

	Superficial gastritis		Normal	
	Extremes	Ave.	Extremes	Ave.
Total mucosa	0.76 - 1.07	0.90	0.60 - 1.14	0.91
Muscularis mucosae	0.06 - 0.14	0.08	0.03 - 0.21	0.07
Gland layer	0.43 - 0.71	0.60	0.39 - 0.91	0.61

The glandular layer was in almost all instances normal in regard to cellular composition, cystic changes, fibrosis, and interstitial infiltration. In one specimen there was complete glandular atrophy, with intestinal metaplasia and the other findings of atrophic gastritis. This specimen contained large amounts of acute and chronic inflammatory infiltrate throughout the mucosa, with many neutrophils, lymphocytes, plasma cells and eosinophils. Four other specimens contained a mild degree of chronic inflammatory infiltration in the lamina propria of the glandular layer. One of these showed aggregation of round cells into pseudofollicles.

The neck stratum (junction of glands and foveolae) was normal in only half of the biopsies which were judged to be characteristic of chronic superficial gastritis. There was significant necrobiosis in the other five (fig. 1). Here the local cellular elements gave evidence of death and necrosis in situ, with simultaneous regeneration. Cellular casts were found in the foveolar lumina of these specimens, plus three others in which necrobiosis was not recognized.

Except for the one instance of atrophy and intestinal metaplasia, the cellular composition of the foveolae was normal. In all but four specimens, however, the lamina propria of the foveolar layer was diseased, and this was the most striking abnormality encountered. Diffuse

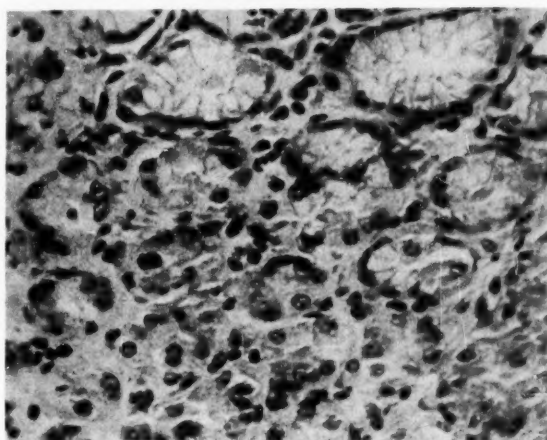


Fig. 1: Necrobiosis of the glandular-foveolar junction (neck) region. In this section local cellular death is more apparent than regeneration.

chronic inflammatory infiltration was striking. Plasma cells made up most of this. In most sections eosinophils were prominent, and in three there were neutrophils mixed in with the chronic exudate. The diffuseness of the process was notable. Areas of edema were common.

Although in all sections there were some areas in which the surface epithelial cells were normal, all, too, showed areas of disease. Nuclear irregularity, pyknosis and scattering were common. Clumps of cuboidal surface cells were frequently interspersed among more normal elements.

COMMENT

It seems fair to state that in most of the cases the discovery of chronic superficial gastritis added a diagnosis which was only incidental to the clinical problem at hand. In two spheres, however, the gastritis appeared to be of unquestioned significance.

Certainly it had been responsible for most of the instances of important hemorrhage. In addition to failure

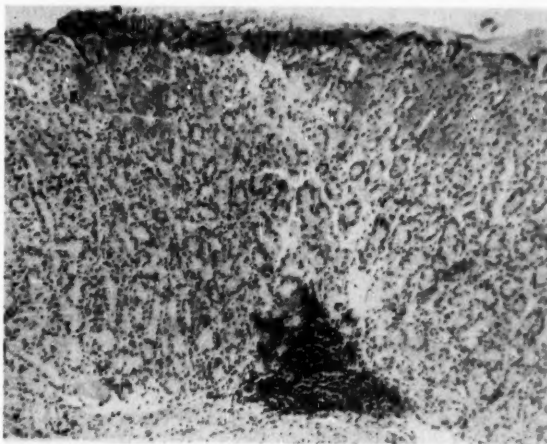


Fig. 2: Fortuitous vacuum tube biopsy of mucosal erosion. The exfoliation has occurred through the neck stratum, with loss of the foveolar layer.

to demonstrate other potential bleeding lesions in nine patients, active hemorrhage was observed gastroscopically from erosions in eleven. Erosions were found in one-third of the patients. There can be little question but that the pathologic process which produces chronic superficial gastritis leads easily to sudden erosive disease. The histopathologic explanation is found in the stratum marking the junction of glands and foveolae: this, the neck region, appears to be the most vulnerable portion of the mucosa (3). Spontaneous exfoliation seems to be initiated here (fig. 2), and, when the process occurs throughout the mucosa, the result may be sudden hemorrhage. Unfortunately, this remains a poorly understood clinical phenomenon because chronic superficial gastritis can be diagnosed clinically only by gastroscopic examination. More important, the ephemeral course of mucosal erosions necessitates gastroscopic examination during the period of bleeding if the true situation is to be recognized. Diagnostic reticence in the face of severe upper gastrointestinal hemorrhage is to be condemned.

Secondly, evidence was obtained to add confirmation to the often reported (1) finding that chronic superficial gastritis may at times progress to chronic atrophic gastritis. It was apparent that the eventual outcome of the superficial process was unpredictable, and that it was not necessarily the mild case which returned to normalcy. In this connection it was interesting to note that biopsies were taken from each of the three patients with achlorhydria: only one showed atrophy of the

glandular elements, the others containing the full complement of secretory cells but severe superficial changes.

SUMMARY

1. Clinical investigation of 83 patients with chronic superficial gastritis revealed that in most cases there were other diseases present which were better explanations for the complaints than the gastritis. It appeared, however, that the gastritis had been particularly important as a source of hemorrhage, by the spontaneous development of multiple mucosal erosions. Serial gastroscopic studies showed that chronic superficial gastritis is often far from a "chronic" process, in some patients changing appreciably within a week.

2. Study of biopsied mucosal specimens indicated that most of the significant microscopic disease was centered about necrobiosis of the glandular-foveolar junctions, with diffuse chronic inflammatory infiltration of the lamina propria of the foveolar layer.

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A STUDY ON THE USE OF PIROMEN® FOR THE TREATMENT OF DUODENAL ULCER IN MAN

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THE PRESENT medical treatment for duodenal ulcer is directed primarily toward reducing acidity and secretion of gastric juice as well as smooth muscle spasm. It is well known that this management is inadequate in the prevention of recurrences of duodenal ulcer. For this reason, we decided to depart from the "cut and dried" treatment with antacids and antispasmodics to evaluate a preparation that would be effective in promoting healing of the ulcer by stimulating a histiocytic, wound healing response. Our past experiences and the literature on pyrogens suggested that these might be effective in promoting healing of the ulcer.

William Beaumont (1), in 1833, was the first to

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Supported by a grant from the Travenol Laboratories, Inc., Morton Grove, Illinois. The Department is in part supported by the Michael Reese Research Foundation.

This study was made at the Indiana State Penitentiary with the cooperation of Warden Alfred F. Dowd and the assistance of Drs. P. H. Weeks and P. C. Traver.

Piromen® is a pyrogenic polysaccharide of bacterial origin; generously supplied by Travenol Laboratories, Inc., Morton Grove, Illinois.

notice that following a fever, gastric secretions became greatly diminished. Meyer and Carlson found that bacterial toxins producing temperatures of 103° prevented hunger contractions (2), and reduced acid secretion (3). Chang (4), in 1933, and Kruger (5), in 1943, found a marked reduction of gastric acidity in patients having high temperatures. It has been known that preparations of enterogastrone and urogastrone that contained pyrogens were more effective in reducing gastric secretion and motility than the purified preparations (6). We found that gastric motility can be inhibited by pyrogens without the rise in temperature (7) and this is also true for gastric secretion (8). Therefore, it is well established that pyrogens can reduce gastric secretion and motility when given parenterally.

Other evidence suggesting that pyrogens would be effective in the treatment of duodenal ulcer was that skin lesions in Piromen® treated rabbits healed more readily, and the scars presented an appearance different from that of the control animals (9). Windle and his group (10) have shown that in animals the transected spinal cords healed more readily when treated with Piromen. McGinty et al. had shown that pyrogens have an ulcer inhibiting action in the Shay rat (11).

The present study was performed at a penitentiary for several reasons, the principle one being that most

TABLE I: HOSPITALIZED GROUP PLACEBO STUDY

Before				After				Gastric Secretion Before and After Placebo Period									
Patient	Symptoms	Physical Findings	X-ray	Symptoms	Physical Findings	X-ray	Days on Placebo	Two 12 Hour Before		Two 12 Hour After		Two Insulin Before		Two Insulin After			
								Vol.	F.A.	Vol.	F.A.	Vol.	F.A.	Vol.	F.A.		
6. K.L.	Epigastric and nocturnal pain	Point tender	Ulcer crater	Epigastric and nocturnal pain	Point tender	Ulcer crater	27	770	54	1142	89	298	20	186	8.8		
13. O.R.	Epigastric and nocturnal pain	Point tender	Ulcer crater	0	0	Ulcer crater	19	816	45	572	0	123	4.7	143	2.3		
14. D.W.	Epigastric and nocturnal pain	Point tender	Ulcer crater	Epigastric pain	Point tender	Ulcer crater	21	625	17	547	35.8	275	25.4	261	22.2		
15. T.O.	Epigastric and gas pain	Point tender	Deformed bulb	Gas pain	General tenderness	Deformed bulb	21	1080	44			348	19	Refused to continue			
16. R.B.	Epigastric and gas pain	General tenderness	Deformed bulb	Gas pain	General tenderness	Deformed bulb	28	1067	47			350	29	Refused to continue			

subjects could have adequate follow-up after therapy. There is a relatively high incidence of duodenal ulcer in the population of the penitentiary, probably as a result of the chronic stress under which the men live. Additional evidence for this chronic stress may be seen in our finding of high uropepsin values in the 12 hour urines of normal inmates and of duodenal ulcer patients (12). This could be the result of an increased release of cortisone by the adrenal gland. Dougherty (13) suggests the possibility that cortisone and Piromen are antagonistic when he demonstrated the antiphlogistic effects of cortisone on Piromen-induced acute inflammation. Numerous articles have appeared showing that cortisone and ACTH can be a factor in reactivating a peptic ulcer (14). Gray and his co-workers (15) have gone a step further and have suggested that peptic ulceration is a result of chronic stress, this being mediated through increased secretion of cortisone. Therefore, a possible new approach to therapy of peptic ulcer would be the use of substances that would counteract the effects of cortisone and ACTH. Pyrogens are well known to produce an inflammatory response, whereas cortisone and ACTH are known to be anti-inflammatory, a directly opposite effect. For these reasons, it seemed worthwhile to attempt to evaluate the effect of Piromen on duodenal ulcer.

This study was carried out in two phases. First, a group of hospitalized patients was investigated and treated. Second, a group of patients was subjected to the same type of study, but their treatment was on an ambulatory basis.

PROCEDURE

All men of the first group were hospitalized for at least four weeks for therapy. They were selected from 125 men with a previous diagnosis of duodenal ulcer made by X-ray and clinical history. From these, 52 men were found to have active symptoms of duodenal ulcer, and they were studied clinically, fluoroscopically, and roentgenologically. An attempt was made to select only those men that fulfilled the following requirements: typical history of active ulcer symptoms; physical findings of localized tenderness in the epigastrium and right hypochondrium; definite active ulcer crater by X-ray; no other symptoms or disease. Several men were included in the study because their symptoms were severe enough to require hospitalization, even though X-ray did not demonstrate an ulcer crater, but other pathology. Therefore, on the basis of severity of symptoms and the necessity of medical treatment, the following additional cases were treated: one case of hypertrophic gastritis, one case of prolapsed gastric mucosa, and several cases of marked deformity of the duodenal bulb. The age of the patients was from 28 to 57 years, with an average of 40 years.

Following a complete physical examination, the men were hospitalized and nocturnal gastric secretion tests and Hollander insulin tests were performed on two consecutive nights. The only change in diet was the addition of protein in the form of eggs, twice a day. No sedation, no antacids, and no antispasmodics were given. Piromen was administered subcutaneously twice a day, usually 10 gammas at 8:00 a.m. and 10 gammas at 8:00 p.m. In order to control side reactions, such as headaches, slight fever, and chills, 10 grains of aspirin

TABLE II: HOSPITALIZED GROUP PIROMEN STUDY

Name	Symptoms	Before		Symptoms	Physical Findings	X-ray	Days on Piromen	Gastric Secretion Before and After Piromen				Piromen Dose in Grammas				
		Physical Findings	Point tender					Vol.	F.A.	Vol.	F.A.		Vol.	F.A.		
1. A.B.	Epigastric and nocturnal pain	Point tender	Ulcer crater	0	0	0	28	932	49.7	1157	64.0	245	17	195	6.0	4
2. B.C.	Epigastric and nocturnal pain	General tenderness	Gastritis	0	0	0	25	660	12.6	872	27.4	181	5.3	150	4.5	4
3. D.E.	Epigastric and L.U.Q. pain	General tenderness	Prolapse gastric mucosa	0	0	0	25	320	10.0	1085	58.9	235	23	216	14.2	4
4. F.G.	Epigastric and nocturnal pain	Point tender	Deformed bulb	Protracted vomiting	Pain and rigidity	Partial obstruction	12	945	51.0			225	20.8	Oper. for obstruction		
5. H.J.	Hiccoughs and abdominal pain	0	Ulcer crater gastritis	0	0	0	44	855	17.6	497	34.0	106	3.6	72.5	5.0	10
6. K.L.	Epigastric and nocturnal pain	Point tender	Ulcer crater	0	0	Deformed bulb	44	1142	89.0	280	17.2	186	8.8	132	6.0	10
7. M.O.	Hematemesis	General tenderness	Ulcer crater	0	0	Deformed bulb	44	330	6.9	332	9.7	67	3.6	60	2.8	10
8. P.R.	0	0	Ulcer crater	0	0	0	44	972	45.5	1257	64.6	151	8.5	145	7.7	10
9. S.T.	Epigastric and nocturnal pain	Point tender	Ulcer crater	0	0	0	14	422	18.4	560	28.0	160	14.8	125	12.0	50
10. V.W.	Epigastric and general abdominal pain	Point tender	Ulcer crater	General abdominal pain	Point tender	Deformed bulb	32	475	11.3	692	37.0	169	9.6	206	11.2	10
11. C.O.	Epigastric and nocturnal pain	Point tender	Deformed bulb	Gas pain	Point tender	Deformed bulb	32	1345	103.0	1400	52.0	305	22.4	180	10.0	10
12. M.C.	Epigastric pain	Point tender	Ulcer crater	0	0	0	32	1682	81.0	1292	76.0	334	22	205	7.5	10
13. O.R.	0	0	Ulcer crater	0	0	0	24	572	0	785	4.7	143	2.3	150	6.0	10
14. D.W.	Gas pain	General tenderness	Ulcer crater	0	0	0	21	620	15.5	547	30.0	270	25	257	18.0	10

were given when necessary. Pyrogen treatment was given usually for a period of four weeks. The patients were then studied once more: nocturnal and insulin gastric secretion studies were made on two consecutive days, and fluoroscopy and X-ray were repeated.

In this group of hospitalized patients, placebos were used on five men for a period of three to four weeks. Three of them were then placed on Piromen without their knowledge. For the placebo study, all procedures, as stated above, were performed. Placebos consisted of the same buffer solution as used for Piromen, and they were given by subcutaneous injection.

A. RESULTS ON HOSPITALIZED PATIENTS

Placebo Study: Table 1 summarizes the results obtained when placebos were used. Symptoms, physical, and X-ray findings are listed for each patient before and after the use of placebos. The initial response of all these men to the placebo was complete relief of symptoms. This was dramatic and made us concerned over the possibility that the placebo had some pyrogenic action. However, after a period of 10 to 21 days, all of the patients except one had recurrence of symptoms. Yet, this one patient still had an active ulcer crater as demonstrated by fluoroscopy and X-ray.

Two of the five patients signed themselves out of the hospital and refused to continue the study because of persistent symptoms. Gastric secretion studies repeated after the period on placebo showed no significant change in either volume or acidity; however, two showed a significant increase in the amount of total mEq. of free hydrochloric acid, whereas one had no free acid.

The following conclusion can be drawn from the placebo study: only one patient had relief of symptoms and no patient had any X-ray evidence of healing of an ulcer crater. Placebo therapy was practically a complete failure, although initially it was able to give complete relief of symptoms.

Piromen Study: Table 2 shows the results with the use of Piromen in the hospitalized group. Of the 14 men treated, 3 continued to have marked symptoms, in one severe enough to require operation for partial obstruction from scarring of the ulcer. The latter patient developed symptoms of obstruction after one week of therapy, and operation was required five days later. Of the 10 other patients with active ulcer craters, 4 showed deformed bulbs, but no active ulcer after therapy. The effect on gastric secretion was not significant in most instances, that is, there was no appreciable change in volume and acidity after treatment with Piromen, except in a few instances. The conclusion can be drawn from the Piromen study that eleven patients out of fourteen were treated successfully, i.e., a 21% failure of Piromen therapy.

Table 3 shows the follow-up evaluation of the 14 patients that had been hospitalized. After the patients had left the hospital, ambulatory treatment with Piromen was given. Five men were maintained on weekly doses of Piromen, and all of them were completely symptom-free and had no physical findings. Of the remaining nine men that did not receive Piromen, only two were symptom-free. It must be emphasized that these men were on full diet, receiving the usual institutional type of meals, including chili, beans, fried foods, etc. Yet, the five men on Piromen treat-

TABLE III
FOLLOW-UP DUODENAL ULCER PATIENTS
AUGUST, 1952

Patient	Follow-up Months	Piromen	Symptoms	Physical	X-ray	Remarks
1. A.B.	9	1 x week	0	0	0	Full diet
2. B.C.	8	2 x week	0	0	0	Full diet
3. D.E.	8	0	Nervous	Tender	0	
5. H.J.	7	1 x week	0	0	0	Full diet
6. K.L.	7	1 x week	0	0	Deformed bulb	Full diet
7. M.O.	7	1 x week	0	0	Deformed bulb	Full diet
8. P.R.	7	0	Psychotic	0	0	
10. V.W.	4	0	Epigastric pain	Point tender		
11. C.O.	4	0	Epigastric pain	Point tender		
12. M.C.	4	0	0	0		
13. O.R.	4	0	0	0		Full diet
14. D.W.	4	0	Gas pain Nocturnal	Tender		
15. T.O.	2	0	Gas pain	Tender		
16. R.B.	2	0	Gas pain	Tender		

TABLE IV
SUMMARY OF GASTRIC SECRETION STUDIES ON PATIENT 6—K.L.

Test	Total Stomach Secretion			Blood Sugar mg%	
	Vol. m.l.	Free m.Eq.	Tot. m.Eq.	Control	30 Min.
12 hour nocturnal, 1st control	760	51.68	60.8		
12 hour nocturnal, 2nd control	780	56.2	71.8		
12 hour nocturnal, after placebo	600	37	49		
12 hour nocturnal, after placebo	1685	131	156.7		
12 hour nocturnal, after Piromen 10 ga.	210	13.5	16.6		
12 hour nocturnal, after Piromen 10 ga.	350	21.0	28.0		
2 hour Hollander, 1st control	354	25.8	30.8	85	40
2 hour Hollander, 2nd control	242	13.6	20.0	72	12
2 hour Hollander, after placebo	162	8.0	10.5	58	16
2 hour Hollander, after placebo	210	9.6	14.0	83	9
2 hour Hollander, after Piromen 10 ga.	116	5.5	7.4	73	6
2 hour Hollander, after Piromen 10 ga.	148	6.4	9.4	78	22

ment remained symptom-free, without requiring the use of any antacid or antispasmodic. The men having symptoms were resorting to Sippy powders, soda bicarbonate, amphojel, and other alkalis, to control their symptoms and, in most instances, without success.

SUMMARY OF TYPICAL CASES

Patient #6, K. L.: A 46 year old white male with a seven year history of gnawing RUQ pain, with nocturnal distress at 1:00 to 2:00 a.m. for the past five years. Definite diagnosis of an ulcer crater was established five years ago. At that time he was placed on Sippy management with a diet consisting of milk, cream, and semi-solid foods. Approximately one year later, he began to have numerous recurrences of ulcer distress. Each exacerbation cleared up under Sippy regime, but the duration of each recurrence has been longer for the past several years. Pain at present is gnawing in character and radiating to the back, relieved occasionally by flexion of the

right leg. He has had occasional black stools and on several instances vomited coffee-ground material. X-ray and fluoroscopy demonstrated an ulcer crater on the lesser curvature of the duodenal bulb with marked point tenderness. Following gastric secretion studies, the patient was placed on placebos for a period of four weeks. He became symptom-free immediately and remained free of pain and distress for about 14 days. At this time he began to complain of cramps after meals and on the 19th day began to have nocturnal distress. On the 27th day of treatment with placebos, gastric secretion studies were repeated. The results are summarized in Table 4. There was no significant change in the nocturnal secretion, but there was some reduction in the secretion to the Hollander test. X-rays were repeated and demonstrated presence of the active ulcer crater. The patient was then placed on 10 gammas of Piromen twice a day, the morning injection given intravenously, the evening injection subcutaneously. By the 6th day of therapy the patient became symptom-free, had no nocturnal distress and slept throughout the night. Secretion

TABLE V
SUMMARY OF GASTRIC SECRETION STUDIES ON PATIENT 1—A.B.

Test	Total Stomach Secretion			Blood Sugar mg%	
	Vol. m.l.	Free m.Eq.	Tot. m.Eq.	Control	30 Min.
12 hour nocturnal, 1st control	835	36.7	46.0		
12 hour nocturnal, 2nd control	1030	62.8	75.19		
12 hour nocturnal, after Piromen	1100	41.8	68.2		
12 hour nocturnal, after Piromen	1215	87.4	104.2		
2 hour Hollander, 1st control	294	224.0	26.5	79	56
2 hour Hollander, 2nd control. Insulin subcutaneously	196	11.56	13.22	90	75
2 hour Hollander, after Piromen 10 ga.	165	2.44	6.13	81	43
2 hour Hollander, after Piromen 10 ga.	225	8.53	13.9	86	22

studies were repeated and there was a marked reduction in the 12 hour nocturnal secretion from an average of 52 to 17 mEq. Since then, the patient has been on Piromen once a week for a period of 16 months. During this period, he has had no recurrence of ulcer symptoms. This is the first time in the past five years that he has been symptom-free for more than six months, that he has been able to eat all types of food, and that he has not needed antacid, soda or antispasmodics.

Patient #1, A.B.: This patient, a 45 year old male, has a six year history of stomach distress consisting of epigastric and nocturnal pain. A year ago, a definite diagnosis of duodenal ulcer was made. He was treated with milk and cream, amphetel, belladonna and sedation. He worked in the prison hospital where he had access to various types of medications which he has used without success to control his symptoms. For the past four weeks he has been awakened at 2:00 a.m. with epigastric pain, radiating from the right to the left side of the epigastrium and to the back. He has had some nausea and vomiting, but no bloody or tarry stools. Fluoroscopy and X-ray demonstrated well localized tenderness in RUQ, the duodenal bulb did not fill out, and a definite ulcer crater was seen on the lesser curvature of the duodenal bulb. The patient was placed on Piromen, 10 gammas subcutaneously twice daily, for a period of 28 days and he became symptom-free on the 10th day. After therapy he had no symptoms, no physical findings, and X-ray showed complete healing of the ulcer crater. Table 5 summarizes the gastric secretion studies on this patient, revealing no significant change in the nocturnal secretion after Piromen. However, there was a questionable diminution of the insulin secretion. Following discharge from the hospital, the patient received Piromen subcutaneously once a week for a period of 9 months. He remained symptom-free during this period. Piromen was stopped at this time. Eighteen months' follow-up shows that he is still symptom-free and has gained approximately 45 pounds in weight. He eats all types of food and takes no medication.

Patient #10, F. W.: This 31 year old white male was first diagnosed as having an ulcer four years earlier. He was treated with diet, Sippy powders, and belladonna. Since then, he has had frequent episodes of epigastric pain and nocturnal dis-

tress. Two years earlier a simple closure was done for a perforated duodenal ulcer, and he made an uneventful recovery. About six months following operation, ulcer symptoms recurred, and once more he was treated with Sippy powders and diet, with some relief of symptoms. At present, epigastric pain is more severe, steady, and cramp-like in nature. Physical examination revealed tenderness in RUQ. X-ray and fluoroscopy demonstrated the crater of an active ulcer in the duodenal bulb. He was treated with Piromen for a period of 4½ weeks. Following this, he still had symptoms of generalized abdominal pain with some point distress. X-rays showed a deformed bulb, but the ulcer crater had disappeared. The patient was placed on amphetel and atropine with some modification of his diet. Four months later, epigastric pain and point tenderness were still present and X-rays showed a clover-leaf deformity of the duodenal bulb. Medical management was continued. Four months later, because of repeated gastric distress, the patient was re-hospitalized. After two weeks on milk and cream, amphetel, phenobarbital, and belladonna, he obtained some relief of symptoms. At his insistence, he was discharged to the prison farm, where medical management was continued. Two months later, he returned to the hospital and was placed in a convalescent ward. Repeated X-rays showed a definite active ulcer crater. The patient refused surgery, and it was decided to treat him intensively with Piromen intravenously, 20 gammas in the morning, 10 gammas at night. After 14 days of this treatment he became symptom-free. The same therapy was continued on an ambulatory basis for four weeks. At this time, he was completely free of symptoms. Then, the patient was X-rayed and fluoroscoped and given a complete physical examination. X-rays showed a deformed duodenal bulb, but no crater. He was discharged from prison and no further follow-up has been obtained.

This patient is considered a failure in regard to response to a small dose of Piromen. However, when an adequate dose was given, 20 gammas intravenously in the morning, 10 gammas intravenously at night, he finally became symptom-free.

B. RESULTS ON AMBULATORY PATIENTS

Men with definite duodenal ulcer were treated on an ambulatory basis, regardless of severity of symptoms.

TABLE VI
PLACEBO STUDY
SEPTEMBER 1952 AMBULATORY

Name	BEFORE PLACEBO				Days Rx	AFTER PLACEBO		
	Symptoms	Physical Findings	X-ray			Symptoms	Physical Findings	X-ray
17. B.W.	Epigastric and nocturnal pain	Point tenderness	Ulcer crater	21	Nocturnal pain	Point tenderness	Ulcer crater	
18. W.R.	Postprandial and nocturnal pain	Point tenderness	Ulcer crater	24	Severe nocturnal pain	Point tenderness	Ulcer crater	
19. Z.K.	Epigastric and nocturnal pain	Point tenderness	Deformed bulb	20	Epigastric pain	0	Deformed bulb	
20. T.R.	Girdle and burning pain	Diffuse tenderness	Deformed bulb	21	0	0	Deformed bulb	
21. L.K.	Epigastric and nocturnal pain	Point tenderness	Ulcer crater	34	Burning and gas pain	Diffuse tenderness	Deformed bulb	
22. K.B.	Burning and nocturnal pain	Point tenderness	Ulcer crater	33	Steady cramps nocturnal	Diffuse tenderness	Ulcer crater	
23. U.O.	Constant burning and nocturnal distress	Point tenderness	Ulcer crater	52	Burning pain	Diffuse tenderness	Ulcer crater	
24. R.N.	Epigastric and nocturnal pain	Point tenderness	Ulcer crater	52	Burning and nocturnal pain	Diffuse tenderness	Ulcer crater	
25. M.D.	Burning and nocturnal pain	Diffuse tenderness	Ulcer crater	44	0	0	Deformed bulb	
26. V.A.	LUQ and nocturnal pain	Diffuse tenderness	Ulcer crater	52	0	0	0	

Our reasons for doing this were as follows: It is well known that, when a patient with active ulcer is hospitalized and receives additional attention, this alone can be sufficient to produce healing of the ulcer, regardless of the type of medication used.

A group of 57 men were all new ulcer patients in the institution, and most had a pre-prison history of ulcer. Once more attempts were made to select only those who showed a definite ulcer crater on X-ray and had typical ulcer symptoms. Thus, 10 men were selected. Medical examination and attention were kept at a minimum, so that psychological effects would be minimized. Therefore, no extensive history or physical examination was made until after the study was completed. The majority were interviewed briefly, and then were placed on subcutaneous placebos for a period of four weeks. All responded favorably with some relief of symptoms for the first two weeks, as shown in *Table 6*. Three had complete relief of symptoms, four had no physical findings of point tenderness, and one had complete healing of his ulcer crater as shown by X-ray. At that time, those that still had symptoms and X-ray evidence of activity, were placed on Piromen for a period of four to six weeks. *Table 7* is a summary of the results on 11 men, 6 of them from the placebo series, that received ambulatory treatment with Piromen. Of the 11 men, 3 still had some abdominal symptoms, though greatly reduced. All showed healing of their ulcer craters, but 7 of the 11 showed deformity of the duodenal bulb.

Table 8 shows the follow-up on 25 duodenal ulcer patients treated with Piromen. The follow-up period

varied from 1 to 18 months after therapy. Seven of the 25 had recurrences within 2 to 12 months after Piromen therapy, a 28% recurrence rate. When Piromen was started again on the 7 patients that had recurrences, 2 did not respond up to the present time, and surgery is being considered for them; the other 5 responded well.

DISCUSSION

It must be pointed out that the only therapy the hospitalized and ambulatory patients received, was Piromen parenterally or, in a few cases, intravenously. No antacids, no antispasmodics, and no sedations were given to any of the patients. However, this does not mean that we advocate the therapy of duodenal ulcer to be restricted only to Piromen. Studies are in progress in which Piromen is used together with an antispasmodic and antacids. Thereby, the ulcer can be attacked by three separate approaches: an antacid to neutralize gastric secretion; an antispasmodic to reduce secretion and motility; and the use of Piromen to stimulate the healing of the ulcer.

The rationale for the use of Piromen can be listed as follows: 1. Its action to promote increased vascularity around the ulcer. 2. As a stimulus to increase growth of immature fibroblastic tissue. 3. Its possible effect as an anti-cortisone. In addition to the above, experimental evidence has shown that Piromen can reduce gastric secretion and gastric motility.

The use of bacterial products for the treatment of duodenal ulcer is not new. Sandweiss and Meyers, in 1934 (16), reported the results of treatment of peptic ulcer with bacterial vaccines, and they reviewed pre-

TABLE VII
PIROMEN STUDY
SEPTEMBER 1952 AMBULATORY

Name	Symptoms	BEFORE PIROMEN		Days Rx	Symptoms	AFTER PIROMEN	
		Physical Findings	X-ray			Physical Findings	X-ray
17. B.W.	Gas and nocturnal pain	Point tenderness	Ulcer crater	34	0	0	Deformed bulb
18. W.R.	Severe nocturnal pain	Point tenderness	Ulcer crater	66	Umbilical distress	0	Deformed bulb
19. Z.K.	Epigastric pain	0	Deformed bulb	37	0	0	0
22. K.B.	Steady cramps, nocturnal pain	Diffuse tenderness	Ulcer crater	56	Gas	0	Deformed bulb
23. U.O.	Burning pain	Diffuse tenderness	Ulcer crater	30	0	0	Deformed bulb
24. R.N.	Burning and nocturnal pain	Diffuse tenderness	Ulcer crater	39	0	0	Deformed bulb
27. L.P.	Epigastric and nocturnal pain	Point tenderness	Ulcer crater	25	0	0	Deformed bulb
28. R.Z.	Postprandial epigastric pain	Point tenderness	Spasm of duodenal bulb	28	0	0	0
29. A.D.	Gas and epigastric pain	Diffuse tenderness	Spasm of duodenal bulb	45	Gas pain	Diffuse tenderness	0
30. Y.L.	Epigastric and nocturnal pain	Point tenderness	Ulcer crater	39	0	0	0
31. D.S.	Epigastric and nocturnal pain	Diffuse tenderness	Ulcer crater	52	0	0	Deformed bulb

vious studies on the use of foreign protein in peptic ulcer therapy. Sandweiss and Meyers considered their bacterial vaccines to produce a foreign protein reaction. In a series of 33 patients they found remission of symptoms in 71% of their patients. They felt that the chief value of treatment with foreign protein was its capacity for initiating remission of symptoms. In addition, they treated their patients with alkalis and ulcer diets and with frequent feedings, whereas our patients received no such treatment.

It must be stressed that Piromen is not a protein, but a complex polysaccharide (17), and therefore therapy with Piromen is not identical with foreign protein therapy. When small doses of Piromen are used, side reactions are minimal, consisting of occasional aching of the joints. With higher doses, and when given intravenously, we have observed temperatures up to 101° and chills. The symptoms were easily controlled by an oral dose of 10 grains of aspirin. The aspirin did not cause any exacerbation of ulcer symptoms.

CONCLUSIONS

1. Twenty-five duodenal ulcer patients were treated both ambulatory and in the hospital with Piromen by subcutaneous and intravenous injection. Nineteen had complete relief of symptoms following therapy, a 76% rate of remissions. In 18 of these, complete healing of the ulcer crater was observed.

2. Fifteen patients were treated with a placebo under similar conditions. Of these, 4 had relief of symptoms, and only 1 had X-ray evidence of healing of the ulcer.

3. Recurrences of ulcer symptoms occurred within 2 to 12 months after cessation of Piromen therapy. Seven patients had no recurrence of symptoms from 18 to 20 months after therapy. The over-all recurrence rate was 28%.

4. Piromen, a complex polysaccharide, is recommended as an adjunct in therapy for duodenal ulcer.

TABLE VIII
FOLLOW-UP ON DUODENAL ULCER PATIENTS
MAY, 1953

Patient	Date of Rx	Follow-up	Recurrence Date	X-ray	Remarks
1. A.B.	Nov. '51	18 months	0	0	Healed
2. B.C.	Nov. '51	18 months	0	0	Healed
3. D.E.	Dec. '51	17 months	0	0	Moderate symptoms
5. H.J.	Jan. '52	16 months	0	0	Healed
6. K.L.	Jan. '52	16 months	0	Deformed bulb	Healed
7. M.O.	Jan. '52	16 months	0	0	Healed
8. P.R.	Jan. '52	16 months	0	0	Psychotic
10. V.W.	Apr. '52	13 months	Aug. '52 (4 mos.)	Ulcer crater	Active
11. C.O.	Apr. '52	13 months	Aug. '52 (4 mos.)	Deformed bulb	Active
12. M.C.	Apr. '52	13 months	0	0	Healed
13. O.R.	Apr. '52	13 months	0	Pseudo-diverticulum of duodenum	Healed
14. D.W.	Apr. '52	13 months	Apr. '53 (12 mos.)	0	Active
15. T.O.	June '52	11 months	Aug. '52 (2 mos.)	0	Active
16. R.B.	June '52	11 months	Mar. '53 (10 mos.)	Deformed bulb	Active
17. B.W.	Nov. '52	6 months	Apr. '53 (5 mos.)	Deformed bulb	Active
18. W.R.	Nov. '52	6 months	0	Deformed bulb	Healed
19. Z.K.	Dec. '52	5 months	0	0	Healed
22. K.B.	Feb. '53	2 months	0	0	Healed
23. U.O.	Mar. '53	1 month	0	0	Healed
24. R.N.	Mar. '53	1 month	0	0	Healed
27. L.P.	Sept. '52	8 months	0	Deformed bulb	Healed
28. R.Z.	Dec. '52	5 months	0	0	Healed
29. A.D.	Dec. '52	5 months	Feb. '53 (2 mos.)	0	Active
30. Y.L.	Mar. '53	1 month	0	0	Healed
31. D.S.	Mar. '53	1 month	0	0	Healed

5. The initial dose of Piromen should be 10 gammas subcutaneously, twice a day, and the dose should be increased depending on the course of the patient. Doses up to 20 gammas intravenously twice a day have been given.

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THE EFFECT OF EMULSIFYING AGENTS (TWEEN 60 AND SPAN 60) ON THE GASTRO-INTESTINAL TRACT

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THE DEVELOPMENT of hexitol-derived emulsifying agents dates back 40 years. However, not until recently has their use in commercial foods and pharmaceuticals become widespread. In the last several years these substances have been employed in preparations for use in such diverse fields as ophthalmology (1), bacteriology (2,3,4), dermatology (5), and gastro-intestinal diseases. In the latter, their use has been limited particularly to those conditions which affect fat absorption (e.g. celiac disease) (6,7,8).

In spite of the rapid accumulation of literature on these agents (9), few reports have been noted dealing specifically with the independent pharmacological action or possible untoward results of these substances.

This study represents an attempt to determine the effect of large doses of two of these agents (Span 60* and Tween 60*) on the alimentary tract of man.

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Supported by a grant from the Atlas Powder Company, Wilmington 99, Delaware.

Submitted April 20, 1953.

*Span 60 and Tween 60 are Atlas Powder Company trademarks for sorbitan monostearate and polyoxyethylene (20) sorbitan monostearate respectively.

PLAN OF STUDY

The study was divided into two parts:

Part I consisted of observations on the effect of prolonged feeding of large amounts of Tween 60 (R) or Span 60 (R) to a group of persons in a home for old people. These observations covered changes in a) the gas pattern of the bowel, b) intestinal motility and c) gallbladder function as evaluated by standard roentgenologic techniques. In addition the subjective symptoms—if any—were also noted.

Part II of this study dealt with acute experiments on hospital patients (Cook County Hospital) who received only one large dose (20 gm.) of either Tween 60 or Span 60. These experiments covered gastric motility, and gastric acidity. Studies on bile flow through a "T" tube were done in patients who had had biliary tract surgery with drainage of the common duct. These patients with biliary fistulas received nine grams of the test substance.

MATERIAL AND METHODS

Part I

The subjects for this study were chosen from patients at the Oak Forest Infirmary, Oak Forest, Illinois. These patients are institutionalized because of degenerative diseases and belong, therefore, mainly in the older age groups. Those selected for this study were first carefully screened—through a detailed history in-

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cluding review of symptoms by system—by one of us (H.M.S.) for obvious gastrointestinal diseases. If no history of gastro-intestinal disease was obtained and the subjects appeared willing and able to cooperate, they were given a complete physical examination and a battery of laboratory tests. The latter included complete urinalysis, hemogram and the following chemical determinations: non-protein nitrogen, creatinine, blood urea nitrogen, total protein, albumin, globulin, alkaline phosphatase, cholesterol, cholesterol esters, thymol turbidity, gamma globulin and bromsulphalein retention*. Any patient showing significant abnormal laboratory findings was eliminated. Patients with gross abnormalities demonstrable by roentgenologic studies including flat plate, barium meal without fluoroscopy and cholecystography were also eliminated. In order to obtain the nineteen patients studied, it was necessary to screen several hundred cases.

The following procedure was uniformly adopted. Each suitable subject was given three grams of either Tween 60(R) or Span 60(R) twice daily by a registered nurse who watched the patients ingest the capsules and charted each dose.

Flat Plate of Abdomen for Gas Pattern

A 14 x 17" film of the abdomen was obtained by standard techniques at the beginning, middle and end of the medication period. The films taken at these various times were checked for the amount of gas appearing in the bowel.

Gallbladder Studies

Gallbladder visualization was attempted by the technique of the Graham-Cole test. In this test, the patient receives in the evening previous to examination an iodine containing compound which is radiopaque. Thereafter, the patient is fasted and in the morning, the concentration of the dye within the gallbladder is visualized by spot films of the gallbladder area. Following

this, the patient receives a fatty meal of eggs and cream and 45 minutes later, another x-ray of the gallbladder area is taken. Emptying of the gallbladder was evaluated by reduction of the size of the gallbladder. The films taken at the beginning and at the end of this study were checked for concentration and emptying of the gallbladder.

Barium Meal

Fluoroscopic examination at the time of barium ingestion was not done. The patient was given a pint of thin barium and standard x-ray films were obtained of the stomach and small intestines immediately after the barium ingestion. Usually four films—two antero-posterior and two oblique exposures—were taken. Six hours later, a 14 x 17" flat plate of the abdomen was obtained to determine the barium passage time, that is, to locate the position of the head of the barium column within the intestine. These studies were repeated after 28 days of medication. All films were interpreted with special regard to passage time, rate of emptying of stomach, amount of gas and barium in the intestine and location of the head of the barium column.

Part II

The subjects used in this part of the study were patients at the Cook County Hospital, who had been hospitalized for a variety of reasons other than gastro-intestinal disease. In the studies on bile flow, all patients, necessarily, had biliary tract diseases for which they had undergone surgery. Two patients in the Span 60 studies were diagnosed as peptic ulcer.

Procedures

1. *Gastric Motility*: The subject was fasted after the previous evening dinner. At 8 A.M. of the next morning a tube with a rubber balloon attached was passed into the stomach. The balloon had a capacity of about 200 cc. The balloon was inflated after its passage into the stomach and gently withdrawn until a tug developed. This confirmed the placement of the balloon in the cardia of the stomach. At this time, the air was permitted to escape. The balloon was now reinflated with only about 10-15 cc of air in order to avoid possible mechanical stimulation from larger amounts, and connected to a water manometer. Continuous recordings were made on a slowly moving Kymograph. A control period of motility was observed for at least 30 minutes and then the test substance, 20 gms. of Span 60 or Tween 60 was administered by mouth, either through the tube or directly by swallowing. Motility was then recorded for another 90 to 120 minutes. The tracings obtained were evaluated for height and frequency of contraction on a scale of 0-3, the latter being considered the most marked.

2. *Gastric Acidity*: Patients were fasted for 12 hours. In the morning, they were intubated with a Rehfuß tube, and the gastric contents were completely aspirated. The tube was left in place and two or three additional aspirations were done every 15 or 30 minutes. After the third aspiration, the patient received the test substance (20 grams made up with water to a total volume of 100 cc) by injection through the tube. Two subsequent aspirations were made at approximately 30 and 60 minutes after the test agent was given. The free

TABLE I

THE EFFECT ON GASTRIC MOTILITY OF INGESTION OF TWEEN 60 AND SPAN 60

Initials	Age	Sex	Diagnosis	Control	After Tween 60
O.B.	31	F	Nodular Goiter	+	+
Ch.M	46	M	Infected Ganglion	+	+
G.P.	30	F	Laceration of Abdominal Wall	++	++
G.J.	21	F	Hemorrhoids	+	+
C.M.	27	F	Cholecystitis	+	+
F.S.	47	M	Hernia	+	+
					After Span 60
V.K.	42	F	Fibroid Uterus	+	+
R.H.	46	M	Wound Infection	+++	+++
L.F.	30	F	Ischiorectal abscess	+	++
L.W.	58	M	Inguinal Hernia	++	++
W.W.	40	F	Hand Infection	+	++

*These results to be reported elsewhere.

TABLE II

Initials	Age	Sex	Diagnosis	Before Medication			After Medication		
				Time in Minutes	Units of Free Acid	Total Acid	Time in Minutes	Units of Free Acid	Total Acid
H. S.	73	M	Bronchiectasis	50	10.0	18.0	20	0.0	2.0
			Emphysema	20	2.0	18.0	35	0.0	8.0
				45	6.0	16.0	25	8.0	22.0
F. C.	49	M	Silicosis	30	40.0	70.0	40	10.0	38.0
				5	24.0	34.0			
				40	14.0	24.0	25	42.0	80.0
J. R.	54	M	Benign Prostate Hypertrophy	25	78.0	100.0	40	60.0	88.0
				10	70.0	96.0			
				30	44.0	62.0	30	12.0	58.0
M. C.	48	M	Chest Pain	15	52.0	92.0	45	18.0	51.0
				1	56.0	78.0			
				30	0.0	12.0	30	26.0	55.0
B. B.	30	M	Recovered Hepatitis	15	32.0	46.0	45	48.0	70.0
				1	19.0	38.0			
				45	0.0	12.0	35	4.2	46.4
H. S.	78	M	Cor Pulmonale	5	6.0	15.0	70	36.0	68.0
				35	10.0	35.0	45	0.0	20.4
				5	6.3	18.0	70	13.2	30.0
J. J.	60	M	Left Hemiplegia	45	0.0	10.0	30	13.2	30.0
				5	10.0	25.0	65	12.0	30.0
				45	0.0	9.0	30	0.0	23.0
S. B.	68	M	Emphysema Bronchiectasis	5	0.0	8.0	65	0.0	6.0
				45	70.0	86.0	30	61.0	75.0
				5	67.0	78.0	65	73.0	82.0
P. P.	36	M	Peptic Ulcer	45	50.0	62.0	30	61.0	71.0
				5	72.0	80.0	60	72.0	78.0
A. K.	60	M	Peptic Ulcer						

and total acidity were recorded. The appearance of the fluid, viscosity, color and clarity were also noted. Free acidity was determined by titration with 0.1 N NaOH using Topfer's reagent as the indicator; total acidity was determined in the same manner using phenolphthalein as the indicator.

3. *Bile Flow*: Patients having external biliary drainage by means of a "T" tube catheter following bile duct surgery were used in this investigation. The amount of bile drained from these tubes in two two-hour periods was measured before the administration of nine grams of the test substance administered over

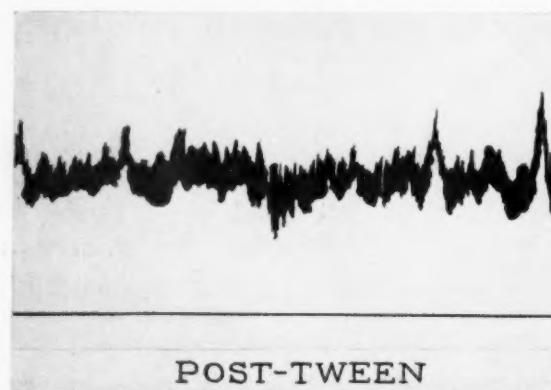
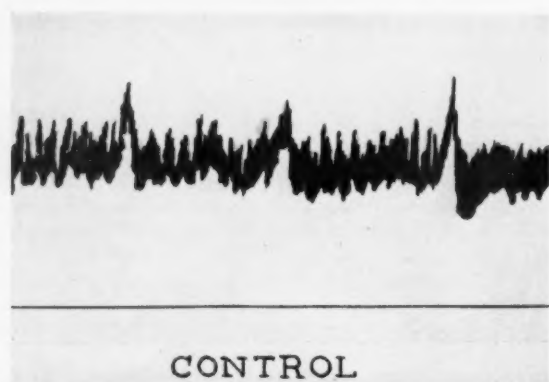


Figure 1

a 24 hour period. Then, similar determinations were again made in two two-hour periods.

RESULTS

Of the ten patients studied who had been given Tween 60(R) for 28 days, four had no change in the intestinal gas pattern, three appeared to have less and three appeared to have more gas at the conclusion of the test period.

In eight patients, no changes were observed in the gallbladder studies, while in two, better concentration, and in one of the latter, better emptying was noted at the conclusion of the study.

There were no significant changes noted in the appearance of the stomach or duodenum in any of the ten patients.

The small bowel pattern appeared the same in four and more normal* in six of the patients at the end of the test period.

At the end of the test period, the progress of the barium meal appeared to be the same in five, slower in one, and slightly faster in four patients.

In the nine patients given Span 60® for 28 days, the following observations were made:

No change was noted in the gas pattern in seven patients. In one, there appeared to be more and in one, less gas at the end of the observation period.

There were no changes in the gallbladder function in seven cases; in one, the emptying time appeared better, and in one, the visualization was fainter.

The stomach appeared unchanged in six patients; in two, it emptied slower and in one case, faster after the medication period.

The intestinal pattern was unchanged in eight pa-

*By "more normal" is meant the absence of "puddling" and the more feathery appearance of the mucosal pattern of the small intestine.

tients. It appeared "more normal" in one patient at the final examination.

The passage of the barium column was unchanged in five patients; it was slower in two and more rapid in two at the end of the test period.

In the eleven patients studied by the balloon technic for gastric motility, no change in motility was noted in the six who were fed Tween 60® (Fig. 1). Of the five patients fed Span 60®, two showed increase in gastric motility (Fig. 2), while in the other three no change was noted (Table 1). Each figure is a 15 minute sample of the control and post-test substance period respectively.

The results in the series concerned with gastric acidity are summarized in Table 2. It will be seen that, as a rule, following Tween 60, there was a slight tendency for both free and total acid to decrease. In one case only, a slight increase in both free and total acid was seen. It may be seen that the changes are rather small and can easily be considered as due to the diluent effect of the material given (100 cc).

Following Span 60®, there was very little change

TABLE III
BILE FLOW IN 2-HOUR PERIODS IN SEVEN PATIENTS
POST CHOLECYSTECTOMY RECEIVING 9 GRAMS
TWEEN 60 ORALLY

Initials	Before Tween		Dose	After Tween	
	0-2 hrs.	2-4 hrs.		0-2 hrs.	2-4 hrs.
D. R.	29 cc.	20 cc.	9 Gm. Tween 60 in 24 hrs.	12 cc.	42 cc.
C. K.	68 cc.	88 cc.	"	42 cc.	41 cc.
J. C.	30 cc.	55 cc.	"	90 cc.	55 cc.
G. M.	120 cc.	60 cc.	"	30 cc.	80 cc.
C. L.	350 cc.	200 cc.	"	60 cc.	60 cc.
A. N.	65 cc.	43 cc.	"	45 cc.	32 cc.
H. P.	130 cc.	67 cc.	"	95 cc.	72 cc.

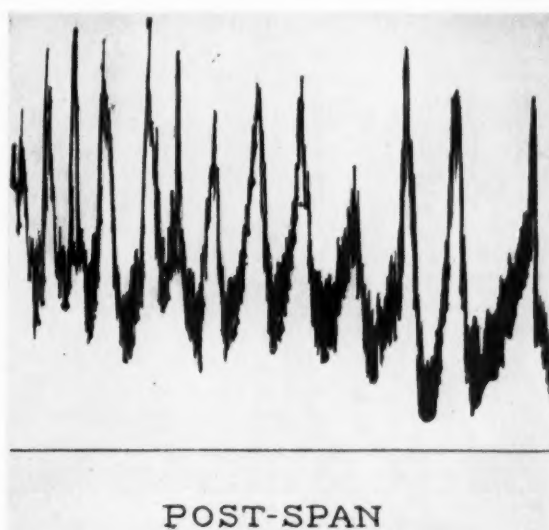
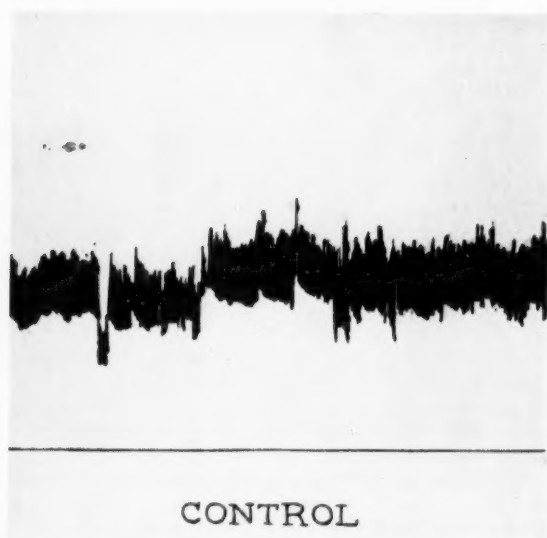


Figure 2

in the free acidity in five cases and a slight increase in one case. The total acidity changed little in four cases and increased slightly in two.

Following both Tween 60® and Span 60®, very little effect was noted on the appearance of the gastric juice as to content of mucus or bile regurgitation. The results seem to be similar whether the tested patient initially had a high or low free acidity.

The effect of the test substances on bile flow could not be evaluated because of the very wide fluctuations in volume in both the control periods and after administration of the test substances (Table 3).

SUMMARY AND CONCLUSION

These gastro-intestinal studies by the methods described above with Tween 60® and Span 60® point to the fact that these substances given in doses of six grams per day for 28 days have no significant effect on the physiologic activity of the gastro-intestinal tract as measured by changes in the gas pattern of the bowel, by gastric emptying time, by passage of barium through the gastro-intestinal tract, and by gallbladder visualization studies.

These studies also indicate that neither Span 60® or Tween 60® in the large doses studied produce any significant changes in gastric acidity or gastric motility.

ACUTE PANCREATITIS

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INTENSIFICATION OF interest in and accumulation of data about acute pancreatitis has contributed greatly to our knowledge of this disease. Yet much remains unexplained. It is our purpose to present all phases of acute pancreatitis only as they apply in clinical practice. Special reference will be made to case material from Brooke Army Hospital including clinical and autopsy studies of 8 fatal cases.

ETIOLOGY

The question of etiology remains a much debated one. While one can attribute certain cases to specific causes, in others one can only note a high incidence of association with certain factors, and in many cases one can find no apparent explanation for the onset of the disease.

The following factors have been found directly and indirectly related to acute pancreatitis:

1. Infection. Pancreatitis has been reported in association with various infections such as mumps, scarlet fever, typhoid fever, etc. (1). Presumably pathogenic organisms reach the pancreas by hematogenous spread.

Case 9, a 30 year old white man was admitted to

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Submitted by the Gastroenterology Section, Brooke Army Hospital, Fort Sam Houston, Texas.

Submitted May 12, 1953.

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Brooke Army Hospital on 16 May 1952 with the diagnosis of mumps involving both parotid glands. On the fifth hospital day, he developed acute severe left upper quadrant abdominal pain radiating through to the back, nausea and vomiting. His temperature rose to 103°F. His white count rose from normal to 18,500 leucocytes per cubic millimeter. Serum amylase was 589 Somogyi units. After three days of intensive medical treatment for pancreatitis the patient became asymptomatic.

2. Gallbladder disease. The high incidence of gallbladder disease in patients with acute pancreatitis has led many workers to suspect a causal relationship. By lymphatic spread of bacteria or by contiguity of duct systems the pancreas may become diseased secondary to the gallbladder infection. At Brooke Army Hospital 42% of patients with acute pancreatitis were proven to have cholecystitis with or without cholelithiasis. This finding corresponds to an incidence of about 50% recorded in most series. Therefore most workers agree that proven gallbladder disease should be corrected surgically when found in a patient who has had pancreatitis.

3. Common channel theory. This theory, first postulated by Opie, (2) was based upon the junction of the common bile duct and the main pancreatic duct into a "common channel" which then empties into the duodenum. With obstruction at the ampulla of Vater by physical means or by spasm, bile may enter the pancreatic duct. Bile itself or perhaps bacteria in the bile activates pancreatic enzymes and causes pancreatitis. While many authors report existence of such a common

channel in 10 to 50% of patients studied clinically or at autopsy, Doubillet and Mulholland found it present in 48 of 49 cases studied clinically (3). There is variance of opinion about the pressure relationship between the biliary and pancreatic systems under experimental and under physiologic circumstances. Howel (4) performed cholangiograms through a common duct tube. Of eighteen patients with known pancreatitis, 14 showed reflux filling of the pancreatic duct and a concomitant elevation of the serum amylase. Two of these patients developed clinical recurrence of pancreatitis. However, Hinton's pressure recording indicates a greater likelihood of flow of pancreatic juices into the biliary tract than of bile into the pancreatic duct (1).

4. Pancreatic duct obstruction. Obstruction to the outgo of pancreatic juices unrelated to the biliary tree may cause increased back pressure, rupture of the pancreatic ducts and inflammation of the gland (5). Obstruction from stone, stricture, edema or epithelial metaplasia of the duct may initiate this cycle. Rich and Duff (5) pointed out that ductal metaplasia may lead to obstruction and localized area of damage. Hinton (1) found such metaplasia at autopsy in 13 of 24 cases of acute pancreatitis. Wainwright (7) found metaplasia of the pancreatic duct and adjacent areas of focal fat in 81 of 2,500 routine autopsies.

5. Neurogenic theory. Exponents of this theory feel that an abnormal reflex arc originates in the pancreas sending impulses to the central nervous system resulting in efferent impulses to the gastrointestinal and other systems. By vasomotor changes or spasm of pancreatic or biliary ducts pancreatitis results. Ayers, Stowens, and Ochsner, (8) also Mallet-Guy and deBeaueu (9) report evidence to support this theory.

6. Trauma. Acute pancreatitis has been observed after blunt, non-penetrating trauma to the abdomen (10, 5). Recently Rini (11) reported 5 cases of acute pancreatitis due to direct trauma.

7. Alcohol. Many patients who suffer recurrent bouts of pancreatitis are known to ingest large amounts of alcohol (5). Also acute attacks are often precipitated by bouts of alcoholism. Dreiling (12) studied duodenal secretions after administering alcohol to 5 patients with chronic pancreatitis and 7 control patients. After intravenous alcohol was given there was no evidence of pancreatic stimulation. When the alcohol was taken orally increase in pancreatic secretion was noted. He feels that the oral alcohol causes increased hydrochloric acid production by the stomach which in turn stimulates pancreatic secretion by producing secretin. The alcohol and hydrochloric acid may cause duodenitis, edema and spasm of the sphincter of Oddi and thus set up the obstructive element which results in rupture of ducts and pancreatitis.

8. Post-surgery. The occurrence of acute pancreatitis after surgery has recently been emphasized (13,14). In abdominal surgery there may be direct trauma to the pancreas. Warren (15) has discussed the question of pancreatitis after subtotal gastric resection. He feels that mild disturbance of pancreatic function is probably frequent, due to vascular injuries, stagnation of duodenal contents and spasm of the sphincter of Oddi as well as injury to the pancreatic ducts or tissue.

Pancreatitis has also occurred without explanation after extra-abdominal surgery.

9. Pregnancy. Acute pancreatitis has been noted in association with pregnancy (16). Apparently a very small percentage of women develop pancreatitis during or shortly after pregnancy. Two patients observed by us developed the first symptoms of pancreatitis in the post-partum period, one immediately and one in the fourth week.

10. Penetrating peptic ulcer. Pancreatitis may occur secondary to a perforating peptic ulcer, or a penetrating ulcer may burrow into the pancreas. This may lead to a severe pancreatitis and collapse or, if there is a slow progressive process, may give no evidence of pancreatic disease. Case 10 was operated upon for removal of a gastric ulcer. At surgery the ulcer was found to have burrowed into the pancreas, a totally unexpected finding.

11. Liver disease. Several clinicians have commented upon the concomitant occurrence of cirrhosis and pancreatitis (17). The relationship between these two conditions, or of both of them to alcoholism and poor nutritional intake can only be speculated upon.

12. Hormonal stimulation. Case 11 developed a typical attack of acute pancreatitis after two days of ACTH therapy for acute rheumatic fever. It is a temptation to consider the ACTH as a causative factor here. It has been shown that ACTH destroys nucleoproteins and also pancreatic acinar cells which contain large amounts of nucleoproteins. The possibility of ACTH as an etiologic or perhaps precipitating factor in pancreatitis warrants further observation.

13. Psychogenic. McCleery (18), in recommending vagotomy for recurrent pancreatitis, postulates that psychic stimuli carried through the vagi may cause increased pancreatic secretion with increased tone of the sphincter of Oddi, resulting in pancreatitis. Emotional factors may well play a role in pancreatic disease, as they have been shown to do in disturbances of other areas of the gastrointestinal tract.

Because of the evidence favoring each of these possible etiologic factors, and because of the benefit obtained by procedures directed toward them, it is probable that one or more of these factors will be important in a given case. The converse is equally true: The clinician must consider the possibility of pancreatitis in all of these situations. Regardless of the cause the pathogenesis of pancreatitis results from activation of pancreatic enzymes with destruction of pancreatic and then surrounding tissues.

CLINICAL PICTURE

Most reports note a somewhat higher incidence of acute pancreatitis in women than men (19, 20). While often discussed as a disease of young people, pancreatitis may appear for the first time in later life. Rose (19) reported 70% of pancreatitis patients had onset of symptoms at 40 years or later. In our series 42% of patients were 40 years or over.

Pain is well recognized as the primary symptom of pancreatitis. Only one patient, who was seriously ill with miliary tuberculosis, did not complain of pain. The most frequent type of pain is a constant ache, but other types such as sharp, cramping, burning are de-

scribed. Pain is usually localized in the upper abdomen, but some patients have periumbilical or diffuse abdominal pain. Thus it is important to consider pancreatitis even though the pain is not in the usual upper abdominal location. Though radiation to the back is a characteristic feature of pancreatic pain, in only 25% of our patients was this present. The clinician must be aware that the pain of acute pancreatitis may closely mimic the zyphi-sternal pain of myocardial infarction, and the right upper quadrant abdominal pain of cholecystitis.

Anorexia, nausea and vomiting are found in most, but not all cases. Hematemesis and melena may occur in up to 10% of patients. Priestley (21) describes hemorrhagic ulceration in the mucosa of the stomach, small intestine and colon. Significant gastrointestinal bleeding was not noted in any of our patients.

The recurrent nature of this disease has been observed by many authors (5, 19, 22). Fifty-four per cent by our patients had gastrointestinal complaints going back several months or several years before admission to Brooke Army Hospital.

The vital signs may or may not be abnormal. In our series the temperature and pulse were normal in about one-half of the patients. The blood pressure was slightly elevated in one patient, slightly depressed in one patient and normal in all others. Shock became prominent during the hospital course of eight patients, all of whom proceeded on to a fatal termination. The significance of shock as a sign of bad prognosis has been noted elsewhere (20).

Abdominal tenderness is present, usually over the area of pain. Board-like rigidity is not common. In only 13% of our patients was a rigid abdominal wall noted. It was not uncommon to find only moderate abdominal tenderness in a patient who was complaining of severe pain.

Jaundice is present in 10-20% of most series. While most patients with acute pancreatitis and jaundice also have gallbladder disease, one cannot accept this second diagnosis without further evidence. Selesnick (23) has studied six cases of recurrent pancreatitis with obstructive type jaundice, without gallbladder disease. However, a normal gallbladder may fail to visualize by the usual roentgenologic methods during and for several weeks after an attack of acute pancreatitis.

In our series, three patients were jaundiced. One of these had gallbladder disease, one liver disease and the third no biliary tract disease.

Though the Gray-Turner and Cullen signs occur only rarely, when present they are suggestive of acute pancreatitis (19, 21, 24). Apparently the slate-blue or gray-brown pigmentation of the flanks or umbilicus is caused by dissection of the pancreatic enzymes into these areas.

DIAGNOSIS

Despite the numerous reports and publications calling attention to diseases of the pancreas, many cases of acute pancreatitis are not being diagnosed until surgery, autopsy or prolonged hospital study. About one-third of the patients studied by Brinkman and Rosenfeld (25) were operated upon for perforated

peptic ulcer. Siler and Wulsin, studying 22 fatal cases of acute pancreatitis, found that in 14 patients, the diagnosis was not made before surgery or autopsy (20). Lipp and Aaron report a 38.6% accuracy of diagnosis (24). In our series pancreatitis was considered at the time of admission in 54% of cases and an additional 25% were discovered shortly after admission. It is significant to note that the admission diagnosis of non-pancreatic disease was often correct but that the clinician did not consider the possibility of associated pancreatic disease. This association obviously should be considered, especially in a patient with gallbladder or liver disease.

LABORATORY STUDIES

The value of serum amylase determinations in the diagnosis of acute pancreatitis is well known. By the commonly used Somogyi method, over 200 units is abnormal. Elevations of the serum amylase have been noted in a number of other conditions such as salivary gland disease, advanced renal disease, perforated peptic ulcer, small bowel obstruction, acute peritonitis and after administration of narcotics (7, 26). However, in most instances of "false positives," the elevation of serum amylase will not exceed 500 Somogyi units. On the other hand a very high amylase value is not required to establish the diagnosis of pancreatitis. In several of our patients the amylase values were between 300 and 500 units, by a comparable method. Since competent laboratory facilities may not be available to the clinician at all hours, it is of practical value to note that a venous blood sample may be drawn and analyzed for amylase determination several hours later, if the specimen is refrigerated during the interval.

Although the serum amylase is often said to return to normal within several hours or several days, it may remain elevated for several weeks without complication or recurrence (27). In our experience, 9 amylase determinations in five different patients were still abnormal after the first week of illness. Because of day to day fluctuations, serial determinations may help to establish the diagnosis.

The rise of serum lipase usually parallels that of the amylase but may remain elevated somewhat longer. By the commonly used Cherry-Crandall method the lipase activity on an olive oil substrate is measured by titrating the resulting fatty acid against 1/20 N sodium hydroxide. Normally the result is less than 1 cc. Above 2 cc. is definitely abnormal. The 24 hour period necessary for its performance represents some limitation to the usefulness of the serum lipase test.

The normally wide variation in urinary amylase excretion requires a time standardization. Probststein (22) has found that a urinary amylase measurement of over 1200 Somogyi units per hour is diagnostic of pancreatitis.

Several other laboratory procedures are helpful in the diagnosis though not specific:

Many observers have noted derangement, usually transient, in glucose metabolism. Hyperglycemia with or without glycosuria may be found (21, 28). Because of edema in the pancreatic head, there may be a mild to moderate increase in the total serum bilirubin. In the inflammatory process there is breakdown in the fat of

the peripancreatic tissue by the liberated lipase. The resultant fatty acids combine with plasma calcium to form insoluble calcium soaps. If the process is severe there will be a marked drop in serum calcium levels, perhaps with tetany, indicating an unfavorable prognosis (See case No. 1 below). This drop in serum calcium level usually is detectable at the end of the first week of illness.

Recently Innerfield, *et al* (29) have reported elevation of the antithrombin titer in patients with acute pancreatitis. This test is not complicated and remains abnormal several days after the disease has begun. If wider usage results in a similar high degree of accuracy, this test will prove an important aid in diagnosis.

Examination of the peritoneal fluid, obtained by abdominal paracentesis with a spinal needle, has been used by Zollinger (30) with helpful results. Of 15 patients with acute pancreatitis they were able to obtain a small amount of abdominal fluid from 12. This fluid was turbid yellow to reddish brown, showed fat globules grossly and microscopically and had an amylase content higher than that of the serum in all 12 cases. In control cases, peritoneal fluid amylase is normally less than 100 Somogyi units (31).

The posterior-anterior chest roentgenogram is to be emphasized for its possible contribution to the diagnosis of acute pancreatitis (24, 32). Abnormalities such as elevation of the diaphragm, pleural effusion, disc atelectasis and pulmonary infiltration are suggestive though not diagnostic of pancreatic disease. Usually seen on the left side, they may occur bilaterally. Schieppati (33) injected trypsin into the retro-peritoneal space of dogs and observed the development of serous or serosanguinous fluid in the left pleural space. The chest findings are thought due to direct spread of the inflammatory process in and beneath the diaphragms. Anterior-posterior roentgenogram of the abdomen may demonstrate pancreatic calcifications, evidence of a chronic process, or it may depict a "sentinel loop" (34). This is a distended loop of intestine, usually small bowel, found in the region of the pancreas. It is thought to be a paralytic ileus due to localized peritonitis. Priestley (21) reports this finding in 68% of patients with acute pancreatitis. Again, this sign is not specific, but is very suggestive of this diagnosis.

The electrocardiogram pattern often shows changes of a non-specific nature but may rarely mimic the changes of acute myocardial infarction (21, 31, 35). These changes are variously attributed to electrolyte imbalance, shock, autonomic nervous reflex.

TREATMENT

In the absence of a complication, the routine treatment of acute pancreatitis should be medical, directed towards several goals:

1. "Pancreatic rest."
2. Relief of pain with secondary Oddi sphincter spasm and vasospasm.
3. Provide adequate fluid and electrolyte intake.
4. Prevent complications of infection.
5. Reverse shock, if present.

With these goals in mind the following outline is followed:

1. Bed rest.
2. Continuous gastric suction to combat vomiting, decompress the stomach and prevent hydrochloric acid from passing into the duodenum.
3. Atropine, 1/100 grain every four hours or Banthine, 50 milligrams every four hours, to block vagal stimulation of gastric secretion, pancreatic secretion and sphincter of Oddi spasm.
4. Oral antacids, after clamping the intragastric tube, to decrease gastric acidity.
5. Papaverine, 1 1/2 grains intravenously every four hours to relieve sphincter spasm.
6. Demerol, 100 milligrams for relief of pain while avoiding the strong sphincter spasm action of morphine.
7. Parenteral fluids and electrolytes as needed for maintenance. One must be alert to the danger of the transient hyperglycemic state that may develop. One must avoid hypoglycemia with its resultant vagus stimulation.
8. Calcium gluconate—10 cc of ten per cent solution intravenously as indicated by blood levels.
9. Antibiotics—penicillin or a wide spectrum antibiotic. Fine (36) has decreased the mortality of experimentally caused acute pancreatitis in dogs by giving Aureomycin. This effect is thought related to decreasing bacterial growth in the intestines, since administration of Aureomycin by gavage saved more dogs than by parenteral injection.

Most patients with acute pancreatitis will begin to respond within several hours to this regimen. If severe pain should continue, several additional methods have been found helpful such as intravenous administration of tetra-ethyl ammonium chloride or procaine, epidural block and paravertebral-sympathetic and splanchnic nerve block (37, 38). While these procedures probably do not affect the disease process they may be most helpful in eliminating the severe pain.

It is generally agreed that surgery should be reserved for the treatment of a complication, such as evidence of suppuration, spreading peritonitis or severe hemorrhage (5, 13, 19, 20, 22). The mortality of surgery in which gallbladder or abdominal drainage is performed is quite high. However, the mortality of surgery in which there is only inspection without manipulation is quite low. Therefore, if the differential diagnosis between pancreatitis and perforated peptic ulcer cannot be made with certainty, diagnostic exploration should be done.

PROGNOSIS

The mortality rate of acute pancreatitis in recently reported series varies from 2 to 20 per cent (13, 19, 20, 21, 28) with medical management. No doubt the ability to detect the presence of mild pancreatitis accounts for much of this wide discrepancy.

AUTOPSY CASES

Some clinical facts may be learned by reviewing briefly 8 fatal cases in this series. In the following three cases, acute pancreatitis demonstrated at autopsy contributed to, but was not the primary cause of death.

Case 1, an elderly man, was brought to the hospital by local police. He was confused, disoriented, and appeared chronically but not acutely ill. On the second hospital day, he was found dead ten minutes after being seen by a ward man to be in no distress. After post-mortem examination, the cause of death was thought to be a right middle lobe lung abscess and pneumonia. The unexpected acute pancreatitis with numerous areas of fat necrosis in the peritoneal fat was considered a contributing factor.

Case 2. An elderly man was hospitalized because of weight loss, hematuria, vomiting and back pain. The course was one of progressive uremia and death. Autopsy examination showed miliary tuberculosis with marked kidney involvement. There was acute and chronic pancreatitis with diffuse peritoneal fat necrosis, not part of the tuberculous process.

Case 3. A 41 year old man, a known alcoholic and cirrhotic, was hospitalized with anorexia, jaundice and abdominal pain. After admission, gastrointestinal bleeding occurred and despite blood replacement and supportive therapy, he progressed to exsanguination and death. At autopsy the pertinent findings included cirrhosis, acute and chronic pancreatitis. The hemorrhage was due to chronic gastritis which, in turn, was secondary to alcoholism, malnutrition and perhaps, also, the pancreatitis. This case demonstrates the not uncommon association of alcoholism, cirrhosis and pancreatitis.

The following two cases occurred as postoperative complications.

Case 4 was a young man who underwent subtotal gastrectomy for refractory postbulbar ulcer. Because the ulcer had penetrated into the head of the pancreas, there was more than the usual amount of trauma to the pancreas at surgery. Twenty hours after surgery, he noted acute severe upper abdominal pain, developed severe dyspnea, and irreversible shock and died on the second postoperative day. Serum amylase was reported as 1200 Somogyi units. At autopsy, there was an extensive, acute necrotic pancreatitis which had eroded the gastrojejunostomy. Ascites, extensive fat necrosis of the mesentery, fat necrosis on both surfaces of the diaphragm, bilateral hydrothorax and compression atelectasis of the lungs were also present.

Case 5, a 29 year old woman, underwent exploratory laparotomy for long standing incapacitating abdominal pain. A catheter was inserted into a cyst-like structure from which bile had been aspirated. Several days later when the tube was found to lie in the duodenum, a second operation was performed to remove it. One day later, the patient developed severe chest pain and shock. After three stormy days, she died. At autopsy, a chronic duodenal ulcer was found to have penetrated into the head of the pancreas setting up an acute hemorrhagic pancreatitis. There was a large retroperitoneal hemorrhage spreading from the pancreas to both kidneys and adrenals. One liter of blood was free in the peritoneal cavity and a bloody effusion was present in the left pleural space.

In the following three cases, the pancreatitis was the primary cause of death.

Case 6, a 36 year old white man, came to the hospital with acute abdominal pain, nausea and vomiting. He had had gastrointestinal symptoms for the past 6 years. After several days in the hospital, the pain became worse, he went into shock, and died. Autopsy revealed acute hemorrhagic pancreatitis with gross blood in both pleural and peritoneal spaces. Microscopic examination showed diffuse metaplasia of the pancreatic ducts with obstruction of the lumina in some areas. Cholecystitis and cholelithiasis were also present.

Case 7. A 55 year old white man was admitted with abdominal pain, nausea, vomiting and somnolence. Twenty-four hours after admission, he suddenly became worse, develop-

ed shock and died about one hour later. Autopsy demonstrated acute and chronic pancreatitis. A small pancreatic cyst had eroded into the pancreaticoduodenal artery causing massive retroperitoneal hemorrhage and death.

Case 8. A 41 year old white male cirrhotic was admitted for severe lower abdominal pain and anorexia. His course was progressively downhill and death occurred after two weeks. This patient demonstrated the frequently described problem of fluid and electrolyte balance which required careful regulation. The blood calcium dropped to 5.4 mg. per cent on the twelfth day of illness and was gradually returned to 9.5 mg. percent on the day of death. Serum amylase values did not exceed 600 Somogyi units at any time. Autopsy showed the expected cirrhosis and severe acute hemorrhagic pancreatitis.

SUMMARY AND CONCLUSIONS

A survey of acute pancreatitis is presented from the clinical point of view.

1. Acute pancreatitis occurs in association with many varied conditions. Those conditions should be looked for in every patient suspected of having pancreatitis. Conversely, when these situations are encountered the possibility of related pancreatic involvement should be studied. This is especially true in patients with gallbladder or liver disease.

2. The typical clinical features of upper abdominal pain with backward radiation, nausea and vomiting are well known. We would emphasize considering the diagnosis of acute pancreatitis although the pain is not of this type or location. Specifically, it may closely mimic the pain of acute cholecystitis or acute myocardial infarction.

3. Laboratory confirmation of diagnosis is obtained through the serum amylase or lipase determination. Recently serum antithrombin level and peritoneal fluid aspiration have been of specific aid in the diagnosis. Roentgenographic findings of "sentinel loop" in the abdominal film or abnormalities at one or both pulmonary bases should be sought for.

4. The treatment of an uncomplicated case should be medical. An outline of therapy is given.

5. Eight fatal cases are briefly described, including autopsy findings. The ominous significance of shock in patients with acute pancreatitis is emphasized.

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SALMONELLOSIS AND SHIGELLOSIS IN COOK COUNTY, ILLINOIS

3. Course of Shigellosis and Salmonellosis Before Microbiologic Diagnosis

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IN ONE OF THE previous communications (1) the distribution of 600 *Salmonella* and *Shigella* strains isolated and typed in the Bacteriology Laboratories of Cook County Hospital between April, 1948 and November, 1950 has been reported. Since then 430 more organisms belonging to these genera were cultured from patients treated in Cook County Hospital, so that the present report concerns itself with 1,030 *Salmonella* and *Shigella* strains isolated between April, 1948 and March, 1953 from persons living in Cook County.

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Submitted May 23, 1953.

DECEMBER, 1953

Tables 1 and 2 show the distribution of these bacterial types.

During this five-year period of observation, *Sh. sonnei* was the predominating organism, followed by *Sh. paradyenteriae* Flexneri II (W), *Sh. alkalescens*, *Sh. paradyenteriae* Flexneri IV (103) and *Sh. paradyenteriae* Flexneri VI (Boyd 88). In some cases the organisms were first isolated from extraintestinal sources, of which the culturing of *Shigellae* from abscess and wound, as well as vagina and blood are of special interest. During the last two years the number of isolations of *Sh. paradyenteriae* Flexneri IV considerably decreased, while types II and VI were seen more frequently than before.

Salmonella typhimurium is the most often isolated

TABLE I
 SHIGELLA STRAINS ISOLATED BETWEEN 1948-1953

<i>Shigella</i> type	No. isolated from			Extraintestinal isolations
	Children	Adults	Together	
sachsi	3	2	5	
ambigua	2	4*	6	* 1 from perinephritic abscess
flexneri I	4	2	6	
flexneri II	84	35*	119	* 1 bile, 1 urine, 1 vagina
flexneri III	4	3	7	
flexneri IV	25	35	60	
flexneri V	1		1	
flexneri VI	26	9	35	
flexneri "VZ"	1		1	
boydii		2	2	
alkalescens	38 ^o	44*	82	^o 1 urine * 1 urine and blood
sonnei	210 ^o	53	263	^o 1 urine
dispar	55	4*	9	* 1 wound
Total	403	193	596	

representative of that genus. *S. typhosa* was second in our material, followed by *S. oranienburg*, *S. montevideo*, *S. enteritidis* and *S. newport*. The primary isolation of *Salmonellae* was mostly from stools. Frequently, however, blood, spinal fluid, urine and pus were the sources. In two cases *Salmonellae* were isolated from the sputum. There was a definite decrease in infections with *S. montevideo* during the past two years, while infections with *S. oranienburg* and *S. enteritidis* were observed more frequently. Contrary to statistics collected before 1948 (2, 3, 4), *S. paratyphi* B was seldom seen in our material compiled between the years 1948-1953.

The relatively high number of typhoid cases may be, perhaps, due to the fact that all patients included in the present statistics were hospitalized persons. We probably missed many cases of salmonellosis which did not seek medical care because of the absence of more serious symptoms.

This inherent defect of epidemiologic statistics that is especially noticeable in reports on intestinal infections, is generally known and does not require further discussion.

It should be added that 21 double and 2 triple infections were observed. The combinations were in children: one case each of simultaneous infection with *S. typhimurium* and *S. oranienburg*, *S. typhimurium* and *S. enteritidis*, *S. muenchen* and *S. senftenberg*, *S. typhosa* and *S. montevideo* (from arthritis), *S. typhosa* and *S. eastbourne* (from blood), *S. enteritidis* and *S. newport*, *S. typhimurium* and *Sh. paradysenteriae* Flexneri IV, *Sh. paradysenteriae* Flexneri IV and *Sh. sonnei*; two instances of *S. typhimurium* and *S. newport*, and three children from whom *Sh. paradysenteriae* Flexneri II and *Sh. sonnei* were cultured. Among adult patients, one each was infected with *S. typhimurium* and *S. newport*, *S. typhimurium* and *S. typhosa*,

S. choleraesuis and *S. anatum*, *S. montevideo* and *S. oranienburg*, *S. typhimurium* and *Shigella paradysenteriae* Flexneri IV, *S. typhimurium* and *Sh. alkalescens* and *S. typhosa* and *Sh. paradysenteriae* Flexneri VI. One person had a suppurative otitis media from which both *S. typhimurium* and *S. montevideo* were isolated, while another had the same strains simultaneously in his stools. The first observed triple infection was caused by *S. typhimurium*, *S. thompson* and *S. newport*, the second by *S. paratyphi* B, *S. montevideo* and *S. anatum*.

Whenever the diagnosis of a *Salmonella* or *Shigella* infection was made in the laboratory, a questionnaire was sent to the physician in charge of the patient. This inquiry was directed to find out the exact age, occupation, alleged source of infection; body temperature, frequency and quality of stools, duration of symptoms, as well as physical status of the patient prior to submitting the first specimen. In other words, in addition to the routine search for clues concerning the source of infection, we tried to collect data on the early course of salmonellosis and shigellosis. In spite of the efforts of the resident staff, only in 477 cases (out of 1,030 diagnosed infections) was it possible to obtain quantitative data on body temperature, number of stools per day, duration of fever and diarrhea. The physical findings reported on the questionnaires were those made by the physician in charge of the patient.

Tables 3, 4 and 5 present summaries of these data. The patients were classified first according to age groups as infants (to 24 months of age), children (to 14 years of age) and adults. The body temperature was registered as afebrile, slight fever (subfebrile) and fever (febrile). Furthermore continuous fever, remittent—intermittent fever and declining fever were distinguished. None of the 477 questionnaires contained data classifiable as ascending fever. Data concerning the numbers of stools were grouped as 0 to 2 per day

TABLE II
 SALMONELLA STRAINS ISOLATED BETWEEN 1948-1953

<i>Salmonella</i> type	No. isolated from			Extraintestinal isolations
	Children	Adults	Together	
paratyphi B	3	5*	8	* 1 blood
typhimurium	88 ^o	56*	144	* 4 spinal fluid, 1 osteomyelitis, 1 wound, 5 blood, * 1 otitis, 1 pneumonia, 1 spinal fluid, 1 urine, 2 blood.
chester	1		1	
derby	4	1	5	
california	1		1	
bredency		2*	2	* 1 blood
choleraesuis	3 ^o	4	7	^o 1 blood
thompson	2	4*	6	* 1 urine
virchow		1	1	
oranienburg	37 ^o	20*	57	^o 2 blood * 1 urine
barcelly		2	2	
montevideo	19 ^o	19	38	^o 1 arthritis
tennessee	1		1	
newport	14	7	21	
muenchen	3	4*	7	* 1 blood, 1 spinal fluid
manhattan	1	1	2	
irumu	1		1	
typhosa	40 ^o	26*	66	^o 13 blood, 1 arthritis * 3 blood, 1 urine
enteritidis	13 ^o	11*	24	^o 1 blood, 1 spinal fluid * 1 blood, 1 wound
berta	1		1	
eastbourne		1	1	
sendai		1*	1	* 1 wound
panama	2		2	
pullorum		2	2	
give	2	2	4	
anatum	7	6	13	
lexington	1		1	
newington	2		2	
senftenberg		2*	2	* 1 pneumonia
solt	1		1	
wichita	1		1	
worthington		1	1	
havana		1	1	
cubana	1	2	3	
cerro		1	1	
minnesota		1	1	
urbana		1	1	
champaigna		1	1	
Total	249	185	434	

TABLE III
PRE-DIAGNOSTIC COURSE OF SHIGELLOSIS

Causative Organism	Age Group	No. Rept.	Body Temperature			No. stools per day			Duration of diarrhea			Stools			Remarks
			0	1 day	2-5 days	1-2	3-5	6-10	1-3	4-7	2-4	w	y	b	
			S	F	S Co Km D	S Co Km D	S Co Km D	P	dys. dys. wks.						
Sachai Q 771	I	1	1					1	1			1			R
Sachai Q 1030	C	1	1					1	1			1			R
ambigua	A	1			1				1						V
Flexneri I	C	2	1		1			2	2						
	A	2			1			2	1			1			
Flexneri II	I	11	2	1	1	1	1	1	3	6	2				1-R, 1-N, 2-V
	C	38	13	4	3	9	1	1	26	8	3	1	1	yr.	2-V, 2-R, 4-N, 1-T
	A	16	5	2	3	1	1	1	8	5	3				2-V, 1-N, 3-T
Flexneri III	I	1			1				1						1-R
	C	4	3	1				3	1	2		1			
Flexneri IV	I	3	1	1	1			1	2			1			1-T, 1-N, 1-R
	C	5	1		4			2	2	2	1	1			2-V, 4-T, 2-F, 1-Ch, 1-Im
	A	22	13	1	2	1	1	1	7	4	10	1	3	mos.	1-R, 1-N
Flexneri VI	I	3	1	1	1			1	2	3					
	C	14	2	3	2	3	1	1	12	1	1	5	1		
	A	2	1					1	1						
Bovdii P 274	A	1			1			1	1			1			F
Bovdii D 19	A	1						1							
alkalescens	I	7	4	1	1			3	2	2	5	1	1		
	C	31	5	1	2	1	1	6	5	7	3	2	4	1	
	A	34	8	2	1	1	1	5	6	3	3	3	1	1	2-V, 3-F, 1-Ap, 1-Im
															1=2 yrs.
sonnei	I	11	5	1	1	2		4	3	3	3	1	6	mos.	1-V
	C	76	18	18	9	22	2	2	4	30	36	6	53	10	5-V, 1-Pn, 8-R, 8-N, 1-Sp
	A	9	3		2	1	2	1	3	3	1	1	4	mos.	1-Pn, 1-T, 2-F, 1-Im
															1=6 mos.

ABBREVIATIONS:

I—infants
Rept.—reported
Co—continuous fever
C—children
S—subfebrile
Rm—remittent fever

A—adults
F—febrile
P—profuse diarrhea
R—upper respiratory tract symptoms
O—afebrile
D—descending fever curve
bru—simulating brucellosis

V—intensive vomiting
T—intensive tenesmus
Ap—simulating appendicitis
Sp—enlarged spleen
Ch—cholecystitis
Im—intermittent diarrhea
dys—days

w—watery
g—green
b—bloody
y—year
N—central nervous system symptoms
F—food handler
Pn—pneumonia

TABLE IV
PRE DIAGNOSTIC COURSE OF SALMONELLOSIS

Causative Organism	Age Group	No. Rept.	Body temperature elevated			No. stools per day			Duration of diarrhea			Stools			Remarks	
			0-1 day			2-3 weeks			1-3			w g b				
			S F	S Co	Rm D	S Co	Rm D	Longer	0-2	3-5	6-10	P	1-3	4-7		2-4
para B	I	1	1					1			1			1		R
	C	1	1					1			1					
A	2		1					2			1			1		
typhimurium	I	8	1	2	1	1	1	1			4	3	1	1	2	1
	C	29	2	9	5	2	7	1	1	2	2	25	1	1	1	1-Im, 2-V, 5-R, 2-T, 2-Sp, 3-N
	A	25	8	6	2	2	1	1	3	2-2 mos.	2	21	1	1	2	2-V, 2-F, 1-T, 2-Sp, 1-Ap, 1-Ch, 1-Im
derby	C	1	1					1			1					
	C	1			1			1			1					1-N
A	3				3			2								
thompson	I	1			1			1			1	1				N
	A	2	1		1			2			1	1				1-F
oranienburg	I	5	1	1	2	1	1	1			1	4		1	1	1-R, 1-N, 1-V
	C	20	4	2	3	5	1	1	2	1-3 mos.	2	16	1	1	4	3-Im, 2-N, 2-V, 1-T
	A	11	4	2	1	1	1	1	1	2-8	1	2	8	1	7	1-2-F, 1-Ch, 1-V, 1-T, 1-R, 1-Sp, 1-Im
montevideo	I	5	1	1	1			1			2	2		1	1	1-R, 1-N
	C	10	2	3	2	1		1		1	8	1		4	3	1-Sp, 1-N, 1-V
	A	12	4	2	3	1		1	1-2 mos.	1	9	1	1	3	6	1-Sp, 1-Ap, 2-F, 1-Im
newport	I	2		2				2			2	3		1	1	1-N
	C	6	1	2	1	1	1	1	1	5	1	2	3	1	1	1-R
A	3	1	1	1	1			3			2	1		1	1	1-T, 1-N
munichen	C	2	1		1			2			1	1				
	A	1	1		1			1			1	1				
typhosa	I	9	1	1	2	1	1	1	1	5	3	1		2	1	2-Sp, 1-Ap, 2-N, 1-Im
	C	16	2	1	1	3	2	2	1	1	1	1	6	4	1	3-Sp, 4-N, 4-R, 2-V
	A	15	2	2	2	4	2	1	1	1	8	4	3	3	4	1-T, 5-Sp, 1-N, 1-Pu, 1-V
enteritidis	I	2	1		1			1		1	1		1	1	1	1-N
	C	8	1	1	2	3		1	1	2	5	1	1	3	2	1-Sp, 1-R, 1-N, 1-V
	A	6	2	1	1	1	1		1	1	5		1	3	1	1-T
panama	I	2			1	1		2			1	1		1	1	
	A	2	1		1			2			1	1		1	1	
pullorum	I	2			1			2			1	1		1	1	
	A	2	1		1			2			1	1		1	1	
anatum	I	2			1			2			1	1		1	1	
	C	3	1	1	1			3			1	1	1	1	1	1-Im
A	4	1	1	1	1			4	1-2 mos.		1	1	1	1	1	R
eubana	I	1	1		1			1			1	1		1	1	
	A	1	1		1			1			1	1		1	1	
arribana	A	1	1		1			1			1	1		1	1	

Abbreviations: See Table 3

(no diarrheic frequency), 3 to 5, 6 to 10, and more. The duration of fever and of diarrhea had to be grouped differently. The appearance of the stool was noted and if very watery, green or frank bloody, registered as such. Finally, patients showing symptoms of upper respiratory disease, pneumonia, disturbances of the central nervous system, vomiting, tenesmus, appendicitis, cholecystitis and enlarged spleen were counted.

Table 3 shows that *Sh. alkalescens* infections have a trend to be less serious than shigellosis caused by other strains. One has to remark, however, that the highest temperature observed during this survey, 105.6° F., was seen in a child having a *Sh. alkalescens* diarrhea. There were 8 cases of chronic shigellosis observed, one of them with an undulating fever course. Stools were less frequently bloody than expected. There was no significant difference among the clinical pictures produced by different *Sh. paradyenteriae* Flexneri strains. *Sh. sonnei* infections were somewhat milder but not significantly different.

The reports on salmonellosis showed an unexpectedly high number of afebrile patients, few enlarged spleens and 9 cases with expressed chronicity. Concerning typhoid fever, the book literally went out through the window. Only a few patients had a fever curve which could be considered typical. Early profuse diarrhea was observed, as well as stools with much blood during the first days of the disease. The number of patients infected with the different strains was too small to draw any statistical conclusions. It seems, however, that any type of initial fever or diarrhea may be expected in infections caused by the most frequent *Salmonella* types.

Table 5, which contrasts the compiled reports on shigellosis and on salmonellosis, shows the following:

1. Shigellosis and salmonellosis occur in all age groups.

2. Roughly 1/3 of the infants and children afflicted with shigellosis and 1/7 of these age groups infected with *Salmonellae* do not have fever in the beginning of the disease.

3. The number of afebrile cases among adults was lower, probably due to the fact that this age group seldom comes to a hospital because of a short diarrhea without fever, while mothers will frequently bring their children when anything abnormal is observed.

4. Fever lasting for more than one week is not unusual in shigellosis or in salmonellosis caused by other *Salmonellae* than *S. typhosa*.

5. Diarrhea with more than 5 bowel movements per day is more frequent in shigellosis than in salmonellosis during the early stage of the sickness.

6. The diarrhea may last long in shigellosis and be of short duration in salmonellosis.

7. Green or bloody stools are not characteristic for an infection with any special bacterial species.

8. Intermittent and other forms of chronic diarrhea are observed both in shigellosis and in salmonellosis.

9. Respiratory symptoms, tenesmus and signs of dis-

TABLE V

COMPARISON OF PRE-DIAGNOSTIC COURSE OF SHIGELLOSIS, TYPHOID FEVER AND OTHER SALMONELLOSES

Causative Organism	Age Group	No. Rept.	Body temperature elevated										No. stools per day					Duration of diarrhea				Stools				Remarks									
			0 1 day		2-7 days		2-3 weeks						0-2 3-5 6-10 P					1-3 4-7 2-4 Longer dys. dys. wks.				w	g	b	Im	R	Pn	F	T	Ap	Ch	Sp	N	F	
			S	F	S	Co	Rm	D	S	Co	Rm	D	L	Longer	0-2	3-5	6-10	P	1-3	4-7	2-4														Longer
Shigella	I	37	13	5	3	5	4	1	1	2	1	1	1		11	16	10		18	11	7	1	9	6		2	3						1		
	C	150	43	26	18	34	14	5	3	3	1	1	2		4	57	75	14	105	24	16	3	30	15	31	1	14	1	7	2			1	14	
	A	67	29	5	3	9	4	4	4	3	2	1	3		14	35	18		24	19	19	5	9	3	18	2	1	7	8	1			1	8	
S. typhosa	I	9	1	1	2	1	1	1	1	1	1	1	1		5	3	1		2	1	1		2	1		1							2	2	
	C	16	2	1	1	3	2	2	1	1	1	1			5	6	4	1	6	4	1		5	4	1	4		2	1			3	4		
	A	15	2	2	2	4	2	1		1	1				8	4	3		3	4			3	3	1		1	1	1			5	1		
Other Salmonellae	I	29	4	3	7	5	5	2	2	1					2	23	4		13	13	1		3	9	2	4		3					6		
	C	81	11	17	15	11	9	5	4	4	1	3			9	65	5	2	44	18	7	3	16	13	6	4	7	6	3			5	7		
	A	73	22	14	7	9	6	5	1	3	2				8	60	2	3	35	18	6	6	17	10	5	3	1	2	2	4	2		4	2	6

Abbreviations: See Table 3

turbance of the central nervous system occur in both diseases.

10. Vomiting was present in about 6 percent of the patients. When observed in an afebrile patient with diarrhea, the clinical picture was difficult to differentiate from coccal food poisoning.

11. Splenic enlargement was found in one case of shigellosis; only in 10 of the 40 patients with typhoid fever but in 9 out of the 183 cases of salmonellosis exclusive infections with *S. typhosa*, before the diagnosis was made.

12. Fourteen of the 155 adults with shigellosis or salmonellosis were professional food handlers, workers in restaurants, food factories, slaughter houses, etc. Such persons are a definitive threat to human health.

When one analyzes these findings, one has to consider the possible reasons for the changes in the early clinical picture of shigellosis and salmonellosis. While the histories of many patients prior to hospitalization are rather vague, one has to face the fact that many receive treatment with sulfonamides or antibiotics when reporting to the physician with diarrhea and/or fever, "on general principles." Such medication often suppresses fever with or without a later relapse, and stops or prolongs diarrhea. Especially penicillin is noted to cause such aberrations from the usual course of the disease (5). On the other hand, one has to admit that much has to be learned about the clinical symptomatology of shigellosis and salmonellosis yet and that clinical pictures considered in the past as unusual may be really the typical images of these diseases. May it be either way, the role of the laboratory in establishing the causative agent is, and will remain at least for some time, of paramount importance.

THE RAPID CONTROL OF UNCOMPLICATED DIARRHEA WITH RESION

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APPROXIMATELY 20% of all patient calls in our practice are for gastrointestinal upset and diarrheal syndrome. We do not feel that this is indicative of the true incidence, because only the more severe cases come to our attention and because each call may represent one of several lost time cases in a family. This report is presented to outline a procedure which we have found appreciably reduces the time lost by our diarrhea patients.

The diarrheas seen in private practice range from violent types with frequent watery stools and with associated vomiting, to increased stool frequency which is only mentioned by the patient when the duration of the condition has made it annoying. Abdominal discomfort and cramps are frequently present and often are the precipitating factor in calling for medical help. The causes are diverse, including enteric infestation, epidemic infection, tainted and grossly contaminated

Statistics showing the distribution of 1,030 *Shigella* and *Salmonella* strains isolated from patients of Cook County Hospital during the period between April, 1948 and March, 1953 were given. The course and the physical findings in 477 of these persons before the diagnosis was established was analyzed.

ACKNOWLEDGEMENTS

The author of this paper is much indebted to Dr. A. V. Hardy, Director of Laboratories, Florida State Board of Health, for recommending this study. He is much indebted to all resident physicians and internes of Cook County Hospital for their excellent cooperation. Special thanks are due to Miss Tama Yoshimura (now Mrs. J. Ishihara, with Boston City Hospital) and Dr. Viola Mae Young (now with the Tropical Research Foundation) for their most valuable help in typing the organisms.

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foods, drug-induced gastrointestinal upset, and serious gastrointestinal disease.

The great majority of cases seen in practice are self-limiting. The patient is made acutely uncomfortable for a few days and wants to get better; he does not care why he is sick. The expense of laboratory diagnosis is prohibitive, unless, in the judgment of the physician, it is justified from the history of the case, the violence of the diarrhea, or the duration of the condition. As a consequence, it is infrequent that we attempt to establish the specific etiologic factors except as is possible from a careful history survey.

The possibility of an underlying gastrointestinal disorder or organic disease is considered during examination and history taking. The suspicion of such a condition calls for special attention and a definite diagnosis.

A severe enteric infection is evidenced by its clinical course, and requires diagnosis and special attention when it does not respond to routine therapy. There

Submitted May 8, 1953.

DECEMBER, 1953

have been great strides made recently in the treatment of these diseases (1) which are encountered only rarely in our suburban practices.

The most frequently encountered diarrheas appear to be communicable and widespread. Calls come from a number of patients at the same time. Often other members of the household have had, or will get subsequently, a gastrointestinal upset of less, or possibly greater, severity. Nausea and, frequently, vomiting and abdominal cramps are apt to be associated. Reimann and co-workers (2) have attempted to find the cause of outbreaks of epidemics of nausea, vomiting and diarrhea without much success. They reviewed the literature but have expressed the opinion that only the severe cases have been reported. It is probable that the syndrome reported by them is similar to the diarrhea most frequently encountered by us in private practice. Reimann (3) recently concluded that more severe outbreaks of this kind can be due to a bacillary infection superimposed on epidemic viral disease. In any case, it must be considered a minor ailment as the mortality rate is zero and the time loss per patient is low, although, in the aggregate, it must amount to a great many man-hours and becomes a distressing Public Health problem.

Diarrhea from tainted or contaminated food may be of all degrees of severity. In the relatively mild cases where hospitalization is not required, again, treatment and not diagnosis is the important point. In fact, in clinical practice, differentiation of the diarrhea of mild food poisoning from other diarrhea is only made if similar symptoms are manifest simultaneously in a group which can trace the common source of infection. Simple over-indulgence is often blamed by the patient on bad food.

Drug-induced diarrhea and vomiting have become well recognized side effects of a number of therapeutic remedies, particularly the broad-range antibiotics. Diarrhea which develops during a course of one of these agents can be very distressing, and if allowed to go unchecked, can linger well after the cessation of antibiotic therapy.

In this report, we are dealing with uncomplicated diarrhea after physical examination has revealed no organic disease and with diarrhea secondary to an organic disease already under treatment. The majority of those without organic cause can be expected to recover in 3 to 5 days. Those with organic background usually do not respond to any remedy, and it therefore is particularly pleasing to include in our successful cases two patients in the terminal stages of bronchogenic carcinoma and one patient with intestinal tuberculosis.

The results obtained by one of us (4) with Resion, a multiple adsorbent preparation, were so gratifying that it was felt we should undertake a controlled study to determine if our enthusiasm was justified. We selected for comparison kaolin 45 grains and pectin 1 grain per tsp., and bismuth subnitrate 7.5 grains and paregoric 5 mls per tsp. The procedure for all patients and with all medications was the same. After a careful history survey and a thorough physical examination we prescribed the medication, two tablespoonfuls immediately and one every two hours. In more severely sick patients, we prescribed two tablespoonfuls statim and one every hour for three or four doses, then one every

two hours. In all cases, one tablespoonful q.i.d. was continued for three days after control had been attained. Bed rest for 24 hours, or until the diarrhea cleared, was recommended. Where abdominal cramps were a major complaint an antispasmodic of the belladonna family was also prescribed. All food except weak tea and clear soup was withheld for the first day, and in many instances only cracked ice was permitted. When nausea and diarrhea were under control, a soft diet was permitted as desired by the patient.

The selection of medication for each patient was made in rotation to eliminate the effect of a change in virulence of the infection with time. The patients with diarrhea related to antibiotic therapy were given the medicament for diarrhea midway between and no nearer than 1½ hours from doses of antibiotic in order not to interfere with absorption.

Results are reported on 150 consecutive cases of diarrhea as encountered in our practices. The patients ranged in age from one year to 80 years, 25 being under 16, and 125 being 16 or over. The apparent causes included dietary indiscretion and contaminated foods but were for the most part infectious diarrheas of unknown origin. Antibiotic gastrointestinal reactions are not included in the tabulations, but are mentioned separately.

RESULTS

In the first 60 cases, it became quickly apparent that the patients receiving Resion were controlled more readily than the patients receiving either kaolin and pectin or bismuth and paregoric. Patients who did not respond within 36 hours were switched to another medication. Patients who did not respond to Resion also did not respond to the other drugs. Failures at 36 hours on kaolin-pectin and on bismuth-paregoric were switched to Resion.

Of the 20 patients on Resion, 16 were controlled within 8 hours and 4 required 24 to 36 hours.

Of the 20 patients on kaolin plus pectin, 8 were controlled between 24 and 36 hours. The rest were placed on Resion, 10 responding within the next 24 hours, 2 not responding.

Of the 20 patients on bismuth and paregoric, 10 re-switched to Resion, 4 being controlled in 8 to 10 hours, and 2 within 24 hours. 4 did not respond.

An additional 90 patients were treated with Resion. 86 were controlled within 8 to 12 hours, 4 were not.

In all, a total of 132 patients received Resion, of whom 108 (80%) were controlled in less than 12 hours. An additional 16 (12%) responded between 12 and 36 hours, and 10 (8%) were not controlled within the 36 hour period. This 8% failure compares with 60% and 50% respectively in the small kaolin-pectin and bismuth-paregoric groups.

None of the preparations alleviated the feeling of urgency experienced by some patients.

Those with antibiotic diarrhea who were placed on Resion did not respond until the antibiotic was stopped. 75% responded within 48 hours of cessation of anti-

notic in comparison to patients treated by other means who continued to have diarrhea 8 and 10 days after the end of antibiotic therapy. At this time we do not know whether the development of antibiotic diarrhea can be influenced by Resion.

DISCUSSION

The controlled portion of this study was cut short because in a relatively small number of cases the differences were clear cut. We felt obliged to our patients to give them what had proved to our satisfaction to be the best remedy available. With the use of Resion, we have been able to control diarrhea within 8 to 36 hours in 92% of 132 cases. In our experience the patients who do not respond within this period do not respond to a longer course. This appears to us to be of great importance for two reasons. First, it is possible for most patients to return to their daily activities within one or two days. Second, it enables us to differentiate much more rapidly the patients who need special care and attention from the 92% who do not. Four of ten patients who did not respond were subsequently found on operation or on necropsy to have had organic lesions.

Resion,* which contains polyamine methylene resin, sodium aluminum silicate, and magnesium aluminum silicate in a palatable vehicle, is an adsorbent type of preparation which has the capacity to bind toxic amines and bacterial metabolites (5, 6, 7). Its effectiveness in these regards is attested to by the rapidity with which it acts. We have found that it is essential to use adequate dosage and have impressed our patients with the necessity for taking full measure. This is sometimes not easy in the presence of nausea, but we have found that chilling a liquid preparation makes it more acceptable to the patient. We therefore recommend that the medications used in this study be kept under refrigeration.

SUMMARY

150 consecutive cases of diarrhea were treated empirically.

The first 60 were divided into three groups, one

*The National Drug Company, Philadelphia 44, Pa.

receiving kaolin and pectin, one bismuth and paregoric and one Resion.

Resion provided the most rapid and thorough relief and was used in failures on the other drugs. The other 90 patients also were treated with the Resion.

The cases were classed as failures if diarrhea persisted after 36 hours. Prolongation of therapy after that time was of no value.

108 of 132 or 80% of the cases treated with Resion were controlled in less than 12 hours, and an additional 16 (12%) were controlled between 12 and 36 hours. 10 or 8% were not controlled within 36 hours, 4 of whom subsequently were found to have organic lesions.

CONCLUSION

In a series of 150 consecutive cases of diarrhea, we have confirmed previous excellent results obtained with Resion, and have outlined a simple method for rapid control of uncomplicated cases.

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ABSTRACTS ON NUTRITION

BOLLIGER, A.: *The adrenals of the koala (phascogaleus cinereus) and their alleged relationship to eucalyptus leaf diet.* Med. J. Australia, June 27, 1953, 917-919.

Mackenzie and Owen, in a study of the glandular system of monotremes and marsupials, were impressed by the rudimentary nature of the adrenal tissue in the leaf-eating marsupials (common possum) and the koala or native bear. Bolliger confirmed the small size of the adrenals in three koalas, but did not think this was sufficient evidence to believe that the eucalyptus leaf diet had anything to do with the fact. Moreover, he

proved that the marsupials in question did not require eucalyptus leaf diet to remain healthy. While the question is admittedly not settled, it would appear doubtful if the eucalyptus leaf contains an adrenal hormone-like substance, as has been imagined since Mackenzie suggested it in 1919.

SAPEIKA, N. AND PARKER, R. G. F.: *Effect of senecio alkaloid, pterophine, on the structure and the ascorbic acid of the rat liver.* So. African J. Med. Sci., 18, 1953, 1-4.

Pterophine is one of the as-yet isolated alkaloids of the poisonous plant, senecio, which has long been

known to be a cause of death in cattle, horses and also in man. The hepatic lesions produced in rats by acute poisoning with pterophine are described. Previous work by other authors is confirmed, to the effect that the ascorbic acid content of the liver becomes increasingly diminished with progressive damage to the tissue.

MUKHERJEE, C. AND MUKHERJEE, S. K.: *Studies in iron metabolism in anemias of pregnancy. I. Serum iron.* J. Indian Med. Assn., XXII, 9, June, 1953, 345-351.

Pregnancy brings about a fall in the level of serum iron in the second half of gestation. Anemia in pregnancy is associated with a greater reduction of the iron level of the serum. The difference between microcytic hypochromic and nutritional macrocytic anemias is not important so far as serum iron is concerned. In pregnancy anemia there is great depletion of the iron stores of the body.

SAINT, E. G., ABRECHT, H. F. AND TURNER, C. N.: *Old age: a clinical, social and nutritional survey of 75 patients over 65 years of age seen in a hospital out-patient department in Melbourne.* Med. J. Australia, May 30, 1953, 757-764.

A wide-angle viewpoint was used in studying 75 aged persons. The nutritional status was judged, apparently, largely upon the results of dietary histories. As might be expected, wide variations in nutritional status were found. In cases where malnutrition existed, poverty was seldom the cause, but rather poor eating habits, alcoholism, or inadequate cooking equipment. Most of the complaints were referable to the gastrointestinal tract. One point of importance emerges from this investigation to the effect that, today, major surgery need not be withheld from the aged persons requiring it.

WEINSTEIN, J. S. AND ROE, J. H.: *The utilization of dextrose, levulose and invert sugar by normal and surgical patients.* Am. J. Proctology, March and June, 1953.

Extensive investigation by the authors indicates that invert sugar (hydrolyzed sucrose, containing equal moles of levulose and dextrose) is a better carbohydrate than either dextrose or levulose for rapid infusions. The tolerance rates, using 50 gram doses, for dextrose and levulose separately, are below 0.75 gm. per kilo per hour. Using invert sugar the tolerance rate is near 1.5 gm. per kilo per hour. Consequently, 50 gms. of invert sugar can be given twice as fast as an equal amount of dextrose or of levulose without glycosuria. Diuresis is much less with invert sugar, which also spares protein and minimizes protein catabolism. For those requiring carbohydrate I. V. feeding it is well to limit each transfusion to one hour. The authors suggest 1000 c.c. of 10 percent invert sugar be given three times a day, at 8 A.M., 2 P.M. and 8 P.M.

WEINSTEIN, A.: *Pregnancy in the diabetic.* Am. Pract. & Dig. Treatment, 4, 6, June 1953, 384-389.

The danger of impending toxemia in pregnant diabetics can be gauged by a hormonal assay of serum gonadotropin levels and urinary excretion of pregnandiol. When such danger exists, stilbestrol should

be used. More than half of pregnant diabetics, however, do not need it. In the pregnant diabetic unusual care should be used to regulate treatment thoroughly. Each community of any size should arrange a central laboratory capable of performing hormone assays.

McCORMICK, W. J.: *Domestic water fluoridation—its pathogenic potentialities.* Arch. Pediatrics, 70, 4, April 1953, 114-121.

McCormick admits the immunity to dental caries conferred in young children by either topical application or ingestion of fluorine in dilution of 1 part per million. However, he presents some evidence that the use of fluorine in water actually produces abnormalities in bone formation and in lipase activity. He suggests the daily use of calcium lactate in 5 to 10 gr. doses for those who wish to avoid these abnormalities. The calcium lactate forms the insoluble fluoride.

GROLLMAN, A.: *The use of oral fat preparations in medicine.* J. Clin. Nutrition, 1-4, May, June, 1953, 302-305.

Two commercial preparations of fat-carbohydrate mixtures are available, Lipomul-oral by Upjohn, and Ediol by Schenley. The first furnishes 4 cal. per ml., the second 5 cal. per ml. By their use a high caloric diet may be supplied in smaller bulk than is otherwise possible. Fat emulsions for I. V. use are under investigation but are not available commercially. Oral fat preparations are of value in depressing the endogenous protein catabolism to a minimum, as in acute renal failure, burns, surgical conditions requiring a liquid diet, tuberculosis, and poliomyelitis, as well as in treating underweight or malnourished persons.

BEAN, W. B. AND VANCE, M.: *Some aspects of the tongue in pellagrous glossitis.* J. Clin. Nutrition, 1, 4, May-June, 1953, 267-274.

Cozymase (which contains nicotinic acid amide in its immediately effective form) produced marked improvement in the pellagrous tongue within minutes to a few hours. Nicotinic acid did the same thing within a few hours to days. Similarly, tryptophane (the "step-child" in the vitamin family) worked rapidly to improve the glossitis. ACTH produced comparatively rapid improvement also. Such agents as crude liver extract, yeast and diet required from 3 to 20 days for improvement. As is well known, improvement of a temporary nature may be obtained merely from rest in bed, although the reason for this is fundamentally uncertain. The authors do not recommend cozymase, tryptophane or ACTH in the treatment of pellagra. Primary reliance rests on a good diet, supplemented with vitamins and the correction of underlying disorders of body and mind. The work is presented as a purely experimental investigation of a subject which requires unusually difficult and prolonged study.

SMITH, N. J. AND ROSELLO, S.: *Iron deficiency in infancy and childhood.* J. Clin. Nutrition, 1, 4, May-June, 1953, 224-286.

Children are prone to iron deficiency because of rapid growth, the low iron content of diets in early life and the occurrence of feeding problems. The authors feel that there are abnormalities in iron-deficiency

states other than those due to the anemia itself. This was suggested by the rapid clinical improvement following intravenous iron even before the anemia had improved.

MEYER, L. M. MCINERY, R. AND RITZ, N. D.: *Intravenous treatment of pernicious anemia with vitamin B₁₂*. J. Clin. Nutrition, 1-4, May-June, 1953, 299-301.

The daily intravenous administration of 0.5 or 1.0 microgram of vitamin B₁₂ to 5 patients with pernicious anemia in relapse induced satisfactory clinical remissions. Erythremic levels were attained in two cases treated for 41 and 87 days with 1.0 microgram of vitamin B₁₂ daily.

HIPSLEY, E. H.: *Dietary "fibre" and pregnancy toxemia*. Brit. Med. J., Aug. 22, 1953, 420-422.

Hipsley reviews the diets and the incidence of pregnancy toxemias in various countries, in peace and in war. He comes up with the seemingly strange suggestion that such toxemias are less common in women using diets that contain more fiber, or roughage. He admits that the roughage articles of diet such as vegetables and fruit contain more vitamins than the high-

energy foods such as carbohydrate, but he apparently does not believe that the vitamin intake is the important factor. He notes, for example, that pregnancy toxemia is very common in beri-beri, but that the use of thiamine has no effect on such toxemia.

SWANBERG, H.: *Fluoridation of water and its relation to cancer*. Miss. Valley M. J., 75, 5, Sept. 1953, 125-128.

Swanberg shows that in Grand Rapids, Michigan, cancer deaths have decreased about 10 percent since the introduction of fluoridation of the water supply in 1945, whereas in the U. S. A. the death rate from cancer has gone up about 16 percent. His point is not to recommend fluoridation as a deterrent of cancer but rather to refute Perkin's claim in the booklet of The Fluoridation Education Society, "The Truth About Water Fluoridation" which attempts to use Grand Rapids statistics of cancer death to support the claim that fluoridation of the public water in that city "tends to speed up the cancer process and thereby produces earlier deaths in cancer patients." The official statistics of Grand Rapids apparently show that the exact opposite of this has occurred during the period under observation.

EDITORIALS

WHITHER NUTRITION?

Sebrell (1) in an inspiring address delivered at the Eighth Annual Meeting of the National Vitamin Foundation in New York City, March 4, 1953, first asks if "the science of nutrition may have reached a point of diminishing returns" and then proceeds to suggest a great many avenues for future scientific approach and to indicate numerous unsolved problems in nutrition.

Some years ago the statement was made that two famous Brothers had "sewed up the abdomen," meaning that there was then very little more that could be accomplished by means of abdominal surgery. In retrospect, there was some truth in this remark because, as we see it, the chief surgical advances in the past decade have been made possible through the advent of chemotherapy, antibiotics, the better use of electrolytes and improvements in anesthesia.

Something of the same philosophy undoubtedly applies to nutrition, as we have known it. For example, the play between endocrinology and nutrition has expanded our horizons. Above all, the biochemical investigation of nutrients promises to make of nutrition a much more potent weapon in medicine, even though the maze of biochemical terms employed does render the science less familiar, and almost strange, to the purely clinical investigator.

Obesity presents one of the greatest challenges today. Many physicians do not subscribe to the current philosophy that obesity is always due to over-eating, but rather suspect that obesity is due to some metabolic fault, still to be discovered.

We have long felt that nutrition plays an as-yet-

undefined role in the development of many chronic diseases.

It is probable that certain individuals have a naturally far greater requirement for certain specific nutrients (or group of nutrients) than others. For example, many cases of anemia that defy classification, and whose causes seem perfectly recondite, respond slowly (or rapidly) to the administration of the B-complex, but not at all to its single elements when used alone.

There are many borderline conditions of ill-health to which none of our trite diagnostic labels apply. These abnormal physiological states not infrequently give way before the power of a good substantial diet. In such cases, we have an improved patient, but we do not have any scientific data of interest, simply because such data cannot be obtained in the present state of our knowledge.

Sebrell wisely remarks,—"There is yet another stage, perhaps least understood in its potentialities for public health: optimum, or ideal nutrition. Untold opportunities for research are implied in the question, what constitutes optimum nutrition and how might it be achieved?"

1. Sebrell, W. H.: New opportunities in nutrition research. National Vitamin Foundation: Annual Report 1952. 15 East 58th Street, New York 22, N. Y.

CANCER DETECTION

The Eugene L. Carey Foundation, Inc., of New York City will undoubtedly serve a useful purpose inasmuch as it is dedicated to early cancer diagnosis. Their brochure points out—what all physicians know—that a high percentage of cancers can be detected by simple,

thorough physical examination. However, the public are not so well aware of this fact. Many surveys have shown that if the patient had only reported his earliest symptoms to his physician, his life could have been saved. Conversely, most of these surveys also pointed

out that the physician was frequently to blame for not making an extensive enough examination. Whether the Carey Foundation is going to work exclusively on the public is not known to the writer of this editorial, but their approach is sound and praiseworthy.

BOOK REVIEWS

PRESENT PROBLEMS IN NUTRITION RESEARCH. Basel Symposium, 1-4, X, 1952. Verlag Birkhauser, Basel: Stuttgart.

Printed in English, French and German, the present volume concentrates upon the theoretical basis of nutrition, so that clinical application of our knowledge had to be omitted. The science of vitamins, begun about 1910, is regarded as the great turning point in nutrition knowledge. In various countries and in different centuries, the distributions of intakes are apparently normal and narrow for calories and only slightly less so for total proteins, a fact which suggests that, for these two nutrients, people tend to get what they need and therefore "to need what they want." However, for calcium and riboflavin and the like, there seems to be no "hunger" bearing any relationship to health requirements.

It is possible for agriculture, using known skills, to produce enough food to feed 4,000 million persons by the end of this century. This in an unusually optimistic assessment of the world-population-food puzzle. The microbiology of digestion is described at length. Free and combined amino-acids in foodstuffs are described. The control of chemicals in food by the health authorities forms an important chapter. The practical significance of vitamins in relation to public health policies, as illustrated by the British experiences during and since the war, is extremely valuable. The use of hormones in nutrition receives adequate coverage. Still other problems of importance are described in this volume, which will be of particular value to all clinicians and nutritionists.

PEPTIC ULCER: PAIN PATTERNS, DIAGNOSIS AND MEDICAL TREATMENT. Lucien A. Smith and Andrew B. Rivers. Appleton-Century-Crofts, Inc., New York.

While the present volume gives due consideration to all aspects of peptic ulcer, the chief attention is given to the nature of pain, especially the pain due to complications, penetration and perforation in particular. The entire problem of medical management is ably handled. For several reasons the book may be regarded as an unusually practical one. The effects of Banthine are evaluated. On the whole, the attitude of the authors is a conservative one on all aspects of the disease. Particularly admirable is their tendency to avoid diets that are extremely restricted.

HUMAN EMBRYOLOGY. Bradley M. Patten. The Blakiston Company, New York 1953, \$12.00.

Profusely illustrated, Patten's second edition has embodied comparatively few changes. Younger stages of the human embryo than ever heretofore available, are described, however, and more attention is devoted to early human implantation. Likewise, the development of the heart is expanded, because now a number of cardiac anomalies are amenable to surgical correction or alleviation. Patten's work, running to 800 pages, brings us up to the minute on a very fundamental branch of medical science.

HEALTH PRINCIPLES AND PRACTICE. C. V. Langton, B.S., M.S., Dr. P.H., Ed. D. and C. L. Anderson, B.S., M.S., Dr. P.H. The C. V. Mosby Company, St. Louis, 1953.

It would appear that there is a great demand for books on health, written for the consumption of college students. The present volume, like most of the others which have appeared in the past decade, emphasizes health as a positive goal, rather than the mere avoidance of the disease. It is well written and approaches the subject from every known angle. While it is naturally not too interesting to the physician himself, it may be recommended without reservation to those "educated" persons who desire knowledge and inspiration in their struggle for health. Without desiring, in the least, to disparage "health books"—and the present volume is as direct and valuable as any which the reviewer has examined,—one wonders sometimes just how effective the current, positive, health promotion via books may prove to be. When one talks to a Professor of health education, one gains the impression, for the moment, that in such efforts lie the chief hope of the world. Fortunately or unfortunately, however, our current emphasis on health as a positive goal, suffers from several interferences. One of the least important is the fact that many readers of such volumes at once consider themselves experts in physiology and clinical medicine. The greatest hurdle, however, is the fact that youth is not *naturally* interested in an analytical description of health. It is philosophically possible that health is one of the many things that escape in direct proportion to our positive desire to grasp it, and this is not meant to be a reactionary attitude. We believe it is merely true.

GENERAL ABSTRACTS OF CURRENT LITERATURE

CATTAN, R. AND FRUMUSAN, P.: *The Vascular Factor in Ulcerous Diseases*. Arch. mal. app. dig. 42, 2-4, 502-32. March 1953.

The vascular theory in ulcer diseases, upheld for the first time a century ago by Virchow, cites auto-digestion of an ischemic zone of the mucous membrane by the gastric juice as a result of obstruction or of a spasm of an arteriole of the stomach.

In a work of an exclusively clinical nature, the authors stress in turn the anatomical, clinical and therapeutic elements which reveal the interference of a vascular factor in the pathogenesis of gastro-duodenal ulcer.

Anatomical factors: The more or less constant lesions of thrombotic endarteritis of the arterioles near the ulcer and in certain really exceptional cases, of extensive thrombosis of the abdominal aorta.

Clinical factors: First of all the authors stress certain analogies between the evolution of ulcerous diseases, angina pectoris, and obliterating arteritis of the lower limbs, disorders which have several common etiological factors: being more common in men, encouraged by smoking and influenced by the emotions. They then endeavor to isolate the elements of a functional vascular semiology in ulcer diseases. A new symptom is described with the help of four observations: epigastric cramp after exercise or intermittent claudication of the stomach, a new manifestation of ordinary ulcerous gastric cramp, which is brought on by effort and which evolves like usual post-prandial cramp. In the light of these symptoms, the authors propose a new interpretation of gastric cramp in cases of ulcer which would not appear to be muscular cramp due to ischemia, similar to heart pains in angina pectoris or to cramp of the calves in obliterating arteritis. They also show ulcer to be frequently associated with vascular ailments: arteritis, angina pectoris, arterial hypertension, arterio-sclerosis, Raynaud's syndrome. Even more suggestive is the very frequent occurrence of factors of mixed ulcerous and vascular heredity. According to these authors the prototype of the true vascular form of ulcerous disease is realized by the giant ulcer of the lesser curvature of the stomach in old people of which the clinical and radiological aspect quite exclusive to it is that of a true impaction of the stomach.

Therapeutic factors: The authors have treated with excellent results a certain number of cases of ulcer by intravenous injections of iodine, as usually administered in angina pectoris and obliterating arteritis. By this method, which can only act on the blood vessels, they obtain the very rapid disappearance of pain, (after four to eight times) without the patient having to rest, and complete radiological cures in three weeks.

More recently and in the same connection, the authors have begun to treat ulcer patients by intravenous injections of heparine in same doses called "dispersive doses" (25 to 50 mgs daily) with very encouraging results.

All these facts, verified by the possibility of creating ulcers experimentally in animals by the obstruction of a blood vessel, establish that a vascular factor certainly intervenes in determining ulcer. The authors however are careful not to uphold an exclusively vascular theory. They in fact show that along with the vascular factor and the hydrochloric-peptic factor, the nervous system plays a part of the greatest importance in this disease and they recall all the arguments which prove the intervention of the vegetative nervous system (vagotonic theory) of lesions of the cerebral trunk (Harvey Cushing) and of psychism (psycho-somatic theory).

The cortico-visceral theory recently elaborated by Bykhor has precisely the advantage of synthesizing all the unilateral theories previously enumerated. According to this theory an ulcer is the local result of a general psycho-neuro-vascular disorder, in which the determining factor is a disturbance of the activity of the superior nervous system. The morbid relationship between an ulcer and vascular affections is explained by the cortico-visceral nature common to all these disorders.

LEVY, M., BRETTE, R. AND RICHARD, M.: *Gastric and Duodenal Ulcers in Man with a Known Etiology*. Arch. mal. app. dig. 42, 2-4, 532. March 1953.

The etiologies invoked at the origin of the peptic ulcer are very numerous. The authors after having discussed many of these believe that gastric trauma, allergic gastritis, chemical or drug-poisoning, professional factors and psychosomatic factors can be considered only as favouring factors of the ulcerous attack, but not as causing factors of the peptic ulcer. They claim as the only causing factors of a peptic ulcer, heredity, lesions of the central nervous system, A.C.T.H.—or cortisone-therapies and extensive burns of the skin.

If the demonstrative cases of peptic ulcers caused by lesion of the central nervous system are very few, they are unquestionable; the nervous lesions either are localized near the neuro-vegetative centers of the brain-ground, or cause a dysfunction of these; more usually they are brain tumors. During the course of these tumors, acute ulcers are noticed, often complicated by hemorrhages and perforations. These ulcers frequently appear in children and seem to be of the same nature as the usual ulcers of stomach and duodenum, but their course is more acute.

It is the same for ulcers appearing during A.C.T.H.—and cortisone—treatments: The cases are still very few, but unquestionable, and also these ulcers are usually acute, and frequently complicated by hemorrhages and perforations.

Consequently it seems that a dysfunction of the neuro-vegetative centers or the endocrine glands can determine a gastric or duodenal ulcer in man.

The ulcers of seriously burned patients are also very rare, but unquestionable; they are often complicated by

hemorrhages and perforations, but it is difficult to make more than suppositions about the cause of their arising.

The authors supply many documents about the role of the heredity in the peptic ulcer. In their own statistics concerning 551 cases of ulcers they find from 21% to 44% of family ulcers. Out of 26 cases concerning ulcerous monozygotic twins related in medical publications, there are 21 cases concerning ulcers developed in both the twins at the same place. In consequence the authors consider the important role of heredity at the origin of the peptic ulcer as absolutely proved, but the exact genetic mechanism of this heredity is still little known.

The peptic ulcer is not usually a local trouble of the stomach, as it was formerly thought. The local influences act only as favouring factors of ulcerous attacks; the decisive factor of the peptic ulcer is very rarely a gross lesion of the diencephalic centers; more often it is a dysfunction of these nervous centers or regulating endocrine centers. All these considerations can but remain conjectures as long as our knowledge on the exact physiopathology of the peptic ulcer will not be better specified.

ALBOT, GUY AND MAGNIER, FRANCOIS: *Muscular Hypertrophy of the Pylorus in Adults: (Myomatous form of fibromuscular atresia of the antrum.)* Archives of Diseases of the Digestive Tract, Tome 42, no. 3, March 1953.

In this report presented at the Congress of French gastroenterologists and based on the study of 21 cases, the authors give first of all a morphological study of muscular hypertrophy of the pylorus; they stress the existence of localized internodular furrows, not between the antrum and the pylorus, but right in the prepyloric musculature; with these furrows occur corresponding radiological spurs which are not always antro-pyloric like those described by Andersen, but which may be prepyloric and situated on the greater or lesser curvature; they then render diagnosis difficult by presenting certain lacunary or corrugated aspects characteristic of incipient epithelioma.

In addition to the elongation of the pyloric canal, there exists a concavity at the extremity of the antrum which together with that at the base of the bulb, described by Kirklin, produces either a pylorus shaped like a pair of brackets or like a double pair of brackets or like brackets placed back to back.

The atypical or troublesome forms are the subject of detailed study: forms extending abnormally towards the prepyloric antrum, multinodular forms producing micro-lacunae and which may simulate an epithelioma, localized varieties very difficult to diagnose in the case of incipient cancer and of which these authors contribute the second known study.

The clinical and etio-pathogenic study considers various well-known etiological problems and discusses the relation between muscular hypertrophy of the pylorus, ulcer, cancer and gastritis; the existence or otherwise of retarded congenital muscular hypertrophy is discussed.

The importance of gastroscopy, which was performed in all cases, and of gastrobiopsy, which enables the existence of gastritis to be shown even before gastro-

scopy can detect it, is borne out by personal observation. Similarly the indications for treatment by antibiotics and for various surgical operations are confirmed.

SBOROV, V. M.: *Viral hepatitis in 1952.* J. Indiana State Med. Assn., 46, 6, June 1953, 496-499.

Just 10 years ago, in World War II, we had just completed our first mass experience with hepatitis. The "serum hepatitis" was due to inoculation with a yellow fever vaccine, in which the virus was suspended in a menstruum of human serum. About 2 to 4 months following inoculation, as many as 10 percent of those receiving icterogenic lots developed hepatitis. The disease continues and is still being studied. Diagnosis is difficult. While epidemic hepatitis usually appears with an abrupt onset of anorexia, nausea and vomiting, the artificially transmitted form of hepatitis (homologous serum hepatitis) may have a very insidious onset with few or no symptoms except dark urine and yellow sclera. There is no single test or combination of tests which will unequivocally point to or away from the diagnosis of viral hepatitis. The two kinds of tests refer respectively, to the excretory function of the liver and to liver cell function. The needle biopsy is of value in distinguishing between medical and surgical jaundice. Antibiotics have not been shown to be helpful. Bed rest and a nutritious diet at present are the cardinal points in therapy. Restriction of fat has not been shown to be beneficial. It is thought that chronic hepatitis and even cirrhosis may follow acute viral hepatitis. The use of gamma globulin as a preventive measure to those exposed to the disease shows great promise of success.

SMITH, R. S.: *Selective radicalism in treatment of carcinoma of the stomach.* Northwest Med., 52, 4, April 1953, 286-288.

Inasmuch as patients do not do so well following total gastrectomies, these should be avoided where possible, and greater emphasis placed on the eradication of lymph nodes and portions of contiguous organs at the time of partial gastrectomy. Radical re-operations now are advocated by many surgeons to combat lymphatic and hepatic extensions. There should be further investigations of techniques for constructing substitute gastric reservoirs for gastrectomized patients.

WEISER, N. J., SPIOTTA, E. AND EKMAN, P.: *Experiences in the diagnosis and antibiotic therapy of amebiasis: an analysis of 50 cases.* Am. Int. Med., 38, 5, May 1953, 1002-1026.

Because of the return to civil life of men who have served in the Far East, the possibility of amebiasis should be kept constantly in mind. Sigmoidoscopy, with immediate examination of specimens of mucus for *E. histolytica* is the most practical method of diagnosis, and the best method of gauging cure. The use of antibiotics for intestinal amebiasis was disappointing as regards cure, also in the production of serious side effects. The use of chloroquine and emetine in hepatic amebiasis was variable, and neither can be recommended over the other.

GUPTA, S. C.: *Sensibility of abdominal viscera and peritoneum.* Calcutta Med. J., 50, 3, March 1953, 83-88.

Recent investigations suggest that the origin of
AMER. JOUR. DIG. DIS.

visceral pain has been placed on a physiological basis. Viscera can no longer be regarded as insensitive, for they show the phenomenon of tenderness even apart from the intervention of the sensitive parietal peritoneum. Visceral pain and tenderness are subserved by afferents contained in the splanchnic nerves. Even the posterior parietal peritoneum derives a similar sensory nerve supply. Omentum possesses no afferent supply so that its lesions produce pain only by secondarily involving the parietal peritoneum. Muscle guard is peritoneo-motor or viscero-motor reflex. Gupta says that "muscle guard" is involuntary, and further claims that this reflex cannot be localized to one side of the abdomen, because the involuntary contractions of abdominal muscles, like those of expression, are bilateral. The one exception he admits is in renal colic where muscular rigidity is unilateral.

ISHII, N. and IIMURA, M.: *Observations on the parasitological findings and transmitting agents of endemic amebiasis*. Yokohama Med. Bull., 3, 5, Oct. 1952, 279-290.

Infection rates for *E. histolytica*, *E. coli*, *E. nana*, and *G. lamblia* were found to be higher in Japan than those before World War II. *E. histolytica* produced immunity in those contaminated with it, but no immunity was conferred by *E. coli* and *E. nana*. Drinking water was not the probable transmitting agent and neither are the raw vegetables which all Japanese eat at every meal. Direct and indirect contacts are certainly the most important transmitting agency of protozoan endemic in Japan, both in the country and the cities.

WEIDEN, S.: *The zinc sulfate turbidity test in the differential diagnosis of jaundice*. Med. J. Australia, March 24, 1953, 364-366.

The zinc sulfate turbidity test described by Kunkel, Ahrens and Eisenmenger (Gastroenterology 1948, 11: 499) is discussed. The normal value for the test (employing 129 normal persons) was found to be 11.4 units (standard deviation ± 2.6). In acute infectious hepatitis the average value was 23.0 units (standard deviation ± 5.8), and in obstructive jaundice the average value was 11.1 units (standard deviation ± 4.7). A value exceeding 28 units was usually obtained in chronic hepatitis either of virus or nutritional origin. The test depends upon the precipitation of gamma globulin at room temperature during a 30 minute period, at the end of which period the turbidity is estimated in the photoelectric colorimeter. The standard for comparison is a suspension of barium sulfate.

ZOLLINGER, R. M. AND SALEEBY, R. G.: *Indications for surgery in jaundiced patients*. J. Indiana State Med. Assn., 46, 6, June 1953, 485-491.

For practical purposes, the indications for surgery in jaundiced patients can be narrowed down to common duct stone, postoperative stricture of the common duct, or cancerous obstruction of the extrahepatic ducts. Silent jaundice from a common duct stone is not unusual. Nausea and vomiting are characteristic of common duct involvement. Jaundice does not necessarily occur in common duct stone. Obstruction due to malignancy produces a jaundice which is by no means always "silent." The history and physical examination

of the patient is still of primary importance. Laboratory tests, if made early and repeated, are valuable in differentiating surgical from medical jaundice. Gray stools, decreased urobilinogen in the urine and elevated blood alkaline phosphatase support the diagnosis of surgical jaundice. Elevated cephalin flocculation and thymol turbidity, poor prothrombin response to vitamin K and low cholesterol esters support the diagnosis of medical jaundice and are reasons for delaying surgery. Surgical risk is decreased by nutritional replacement by forced feeding with the addition of bile or Tween 80 and accurate replacement of blood volume.

CREGAN, J. AND HAYWARD, N. J.: *The bacterial content of the healthy small intestine*. Brit. Med. J., June 20, 1953, 1156-1159.

The authors investigated the bacterial flora of the small intestine, using samples removed from the lumen of the bowel with a syringe at gynecological operations. It was found that the whole length of the small gut contains only a transient flora, chiefly of Gram-positive species that are more commonly associated with the mouth than with the large intestine. From the apparent inability of these organisms to become resident in the small bowel it is deduced that an antibacterial mechanism, distinct from the stomach mechanism, must be operating here. The nature of the antibacterial mechanism is unknown.

CHHETRI, M. K.: *Studies on hemorrhagic complications in enteric fever, with special reference to plasma prothrombin*. Calcutta Med. J., 50, 3, March 1953, 95-103.

The author studied the prothrombin levels in the plasma in 100 cases of typhoid fever and found that the prothrombin forming function of the liver was depressed in this disease. This depression was not related to vitamin K deficiency, but it accurately reflected the progress of the case. When the reduction in prothrombin is severe, it is a contributing factor to the hemorrhages characteristic of the disease. The only rational way of treating this deficiency is blood transfusion.

PALMER, E. D.: *An attempt to localize the normal esophagogastric junction*. Radiology, 60, 6, June 1953, 825-831.

As a result of x-ray studies on 15 normal adults following transesophagoscopy attachment of silver brain clips to the esophagogastric line of epithelial change, it was concluded that a portion of the normal resting "abdominal esophagus" is lined with gastric mucosa and must therefore be considered stomach. The location of the esophagogastric junction varies considerably in its relation to the bony landmarks, according to the general body configuration of the individual. The tubular gastric segment which extends up into the esophagus may measure as much as 3 cm. in length in the resting state, but it can be obliterated to become part of the wall of the stomach proper, by distention of the gastric fundus. The mucosa of the esophagogastric junction region seems to be mobile over the underlying tissues, and to be capable of considerable automatic migration, through simple longitudinal contraction of its muscularis mucosae.

PEARSON, C. C.: *Newer concepts in the management of hepatitis and cirrhosis*. Bull. Mason Clin., 7, 2, June 1953, 37-42.

Pearson states that there is no specific agent for the relief of hepatitis or cirrhosis. Over-enthusiastic use of so-called specific therapy may produce alterations harmful to the patient. Person to person contact is the mode of spread of hepatitis. The army in Korea has shown that, in the young healthy adult with hepatitis, it makes little difference whether early ambulation is used or not. In civil practice, however, bed rest is the safest mode of management. Antibiotics, especially aureomycin, when used in moderation, seem to be beneficial, but the use of large, continued doses may adversely affect the liver. ACTH and Cortisone should be used only in fulminating cases as a temporary measure, because they do not actually change the course of the disease. Sodium restriction is valuable in ascites. Cation exchange resins should be used cautiously, and this applies to the administration of ammonium chloride, because the liver cannot convert it to urea.

EPPELSON, D. P. AND WALTERS, W.: *Spontaneous internal biliary fistulas*. Proc. Staff Meet. Mayo Clinic, July 1, 1953.

Only one percent of all patients undergoing operations on the biliary system at the Clinic between 1945-50, had spontaneous internal biliary fistulas. Most of them are due to gallstones and are located between the gallbladder and duodenum. Diagnosis is seldom made prior to operation. Treatment consists in disconnecting the fistula, closure of the intestinal opening, cholecystectomy and careful exploration of the common duct. The operative mortality did not exceed that for cholecystectomy alone. The use of cholangiography at the time of operation is not necessary.

HOFFBAUER, F. W., MCCARTNEY, J. S., DENNIS, C. AND KARLSON, K.: *The relationship of chronic ulcerative colitis and cirrhosis*. Ann. Int. Med., 39, 2, Aug. 1953, 267-283.

Twelve cases are described in which chronic ulcerative colitis and hepatic cirrhosis were associated. These cases were selected from 287 patients with ulcerative colitis seen during an 18 year period. The relationship between the two diseases is quite obscure, but the frequency of the two diseases occurring together may be greater than is appreciated. The possible relationship of viral hepatitis to colonic bacteria is one of considerable importance and interest.

KIER, J. H., GENDEL, B. R. AND RICH, J. R.: *Perforated peptic ulcer during cortisone administration*. Am. Pract. & Dig. Treat., 4, 8, Aug. 1953, 510-511.

A case is reported of perforation of a duodenal ulcer during cortisone treatment for rheumatoid arthritis. It is probable that the ulcer existed prior to the treatment. He recovered following an emergency operation. Later, intra-articular injections of compound F were used without any recurrence of abdominal symptoms. It is considered that, in using cortisone or ACTH on anyone, the possibility should be remembered, that an

existing ulcer may perforate and that even a peptic ulcer may be initiated. This therefore increases the already-known hazards of employing these products.

FRIEDMAN, A.: *Experiences in 289 cases of infantile diarrhea in a nutritionally deficient group of infants*. Am. J. Dis. Child., 85, 6, June 1, 1953, 675-687.

In 289 cases of diarrhea in infants under 2 years of age, an actual mortality due to the diarrhea of 9 percent was experienced. The bacteriological examination of the stools usually showed microorganisms whose connection with the disease was doubtful. However, par-enteral infection seemed to play a definite role in 58 percent of cases. The vast majority of cases showed hypoproteinemia, the serum albumin being less than 4 gm percent. Thirty percent had associated rickets. Intravenous fluids formed an important part of the treatment, sodium lactate being used to overcome acidosis. Feeding was begun as soon as vomiting stopped, irrespective of the continuance of the diarrhea. Buttermilk, or 30% half milk was used, the former proving to be better. Sulfonamides were generally used, but streptomycin, penicillin, aureomycin and chloromycetin also were employed where necessary. The results appear to be good, considering the fact that most of the infants were grossly malnourished and deficient.

MCNAUGHT, W. AND STEVENSON, J. S.: *"Coliform diarrhea" in adult hospital patients*. Brit. Med. J., July 25, 1953, 182-184.

Considerable is known about specific types of bact. coli in infantile stools but less about adults. During the examination of 894 fecal specimens from adult hospital patients, type-specific strains of bact. coli were isolated from 15 cases. Twelve of the 15 cases had diarrhea of varying severity; two of these patients died, the associated organisms being bact. coli 026.B6 and 0.111.B4. It is suggested that such specific disease be called "coliform diarrhea."

SNOW, D. J. R.: *Infective hepatitis: an analysis of 1,000 consecutive notifications in Western Australia*. Med. J. Australia, June 13, 1953, 838-840.

Snow, after analyzing 1,000 cases of infective hepatitis, finds that the mode of spread during the epidemic has been by the transference of particulate feces from person to person.

ROBINSON, B.: *The role of nervous factors in the causation of peptic ulceration*. Med. J. Australia, May, 1953, 624-627.

Robinson goes into some detail about nervous factors in peptic ulcer. While organic nervous lesions are rare in this disease, "psychological deviations" are common and related in part to the importance of the alimentary canal in the emotional life of the individual. Psychotherapy is valuable before ulceration has occurred. Even after ulceration is present the patient should be shown that emotional control is more fundamental than any other form of clinical treatment.

A. H. ROBINS CO., INC.

Appointment of William Allen Smith as plant superintendent of the A. H. Robins Co., Inc., ethical pharmaceutical house of Richmond, Va., has been announced by E. Claiborne Robins, company president. The new superintendent came to the Robins Co. from the Valentine Co. where he had worked for the past eight years in the same capacity. Previous to that he had been with the William S. Merrell Co. for 20 years. Mr. Smith is married and has three children.

SOMOGYI GETS BISCHOFF AWARD AT CLINICAL CHEMISTS MEETING

Pioneer in Sugar Metabolism, Now 70, Continues Study to Help Physicians Make Earlier Diagnosis of Diabetes

Chicago, Ill.—Dr. Michael Somogyi, one of the world's leading biochemists and a pioneer in the study of sugar metabolism, was recently presented with the 1953 Ernst Bischoff Award of \$500, at the fifth annual meeting of the American Association of Clinical Chemists, held here at the Conrad Hilton Hotel.

The Association is composed of 500 clinical chemists, most of whom serve on hospital staffs as increasingly important members of the medical science "teams," aiding physicians in diagnosis and treatment of diseases. Approximately 250 were expected to attend the various functions of the meeting which closes tomorrow.

The Ernst Bischoff Award is given annually by the association on behalf of the company of the same name, located in Ivoryton, Conn., and manufacturers of biologicals and pharmaceuticals. In addition to the monetary award, a bronze medal and scroll were presented to Dr. Somogyi. H. C. Terwilliger, president of the firm, instituted the award to deserving clinical chemists in 1952.

Dr. Somogyi has been in charge of research and chemical laboratories at the Jewish Hospital of St. Louis since 1926. He was formerly instructor in biochemistry at the School of Medicine, George Washington University, St. Louis, fol-

lowing years of research and teaching at Cornell and laboratories in Budapest. He was born in Austria in 1883 and received his Ph.D. in Hungary.

A pioneer in the metabolism of carbohydrates and ketone bodies, he introduced many of the methods now standard in clinical chemistry. He has been widely published on such subjects as diastases, physiology of insulin action, clinical studies of diabetes and analytical methods. He was already studying the problem of sugar metabolism in 1920, when Banting and Best showed a practical way to prepare insulin and won the Nobel Prize.

At the Association dinner, Dr. Somogyi spoke on the "story of insulin and the chemist's role," from the time of the first crude preparations before 1920 until today, when a crystalline preparation is available for control of diabetes. He described the various stages of purification and stressed the clinical chemist's function as an aid to physicians in their clinical applications of the preparation.

Earlier in the day, the meeting had opened with an all-day symposium on Electromigration in Stabilized Electrolytes, held in the Normandy Lounge of the hotel. Study of electromigration helps to determine the different types of proteins in the plasma. Gamma Globulin, for example, is now being studied by means of this procedure. Eleven scientific papers were read. Presiding was Dr. Hugh J. McDonald, Loyola University Medical School professor of biochemistry and newly elected president of the Association.

The International Academy of Proctology announces the establishment and award of a one year Proctologic Research Fellowship in the amount of \$1200.00. This Research Fellowship grant has been awarded to the Jersey City Medical Center, New Jersey, to be administered under the direction of Dr. Earl J. Halligan, Surgical Director of the Medical Center.

Dr. Halligan is a former International President of the Academy. The Board of Trustees of the International Academy of Proctology will vote another Fellowship grant

of a similar amount at the time of the next Annual Meeting of the Academy. Thus, there will be at least two Research Fellowship studies in progress, in different institutions, under the auspices of the International Academy of Proctology.

From: The International Academy of Proctology, 43-55 Kissena Blvd., Flushing, New York.

IMPROVED TRIBIOTIC OINTMENT NOW BEING DISTRIBUTED

A new improved Tribiotic Ointment for the treatment of mastitis in dairy cows and milk goats is now being distributed by Wyeth Laboratories, it was announced recently.

Dr. Richard A. Huebner, director of veterinary service for the pharmaceutical firm, said no change was being made in the medications; penicillin, dihydrostreptomycin and bacitracin are considered capable of inhibiting virtually all mastitis-causing organisms on contact.

The ointment base in which the antibiotics are suspended has been improved, the doctor explained. The new base is miscible (emulsifies rapidly) in milk at the cow's body temperature, and uses the milk as a carrier to spread through the tissues of the udder segment. By contrast, greasy bases ordinarily used cause the medicament to concentrate in or near the point of application.

Practicing veterinarians have been testing the new Tribiotic Ointment in four states since late July. There have been several reports of cows responding favorably under Tribiotic therapy after the disease resisted other treatments, Dr. Huebner said.

Tribiotic Ointment is packaged in one-pinch applicator tubes, for instillation through the streak canal in each teat. Because the combined action of the three antibiotics is much greater than the sum of their separate actions, Tribiotic has been widely used by dairymen since it was introduced early in 1952.

Suggested retail price per tube is 89 cents.



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**ARALEN BENEFITS 16 OF 21
CASES OF LUPUS
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Results of a study have shown that Aralen, chloroquine diphosphate, is valuable in the treatment of discoid lupus erythematosus. Aralen is supplied by Winthrop-Stearns Inc.

The study was conducted by Drs. Leon Goldman, Donald P. Cole and Robert H. Preston, Cincinnati, Ohio, who report their findings in the *Journal of the American Medical Association* (152:1428, August 8, 1953). Aralen was found to be effective in treating 16 of 21 patients suffering from lupus erythematosus, including the localized and disseminated chronic discoid forms and the subacute disseminated type.

Of the 16 benefited, 14 showed "great improvement" and two were helped moderately, with the average duration of therapy ranging from seven to 11 weeks. Patients were observed for six months.

Aralen was selected for testing, according to the investigators, "because it is distinctly less toxic, may be found in the skin in appreciable amounts after oral ingestion, and does not discolor the skin as does Atabrine." They add that "a review of the literature and our own experience revealed that the toxic effects of Aralen are insignificant."

Average dose during treatment was 0.25 gm. twice daily for one or two weeks, followed by 0.25 gm. daily for four to six weeks.

**FRIEDMAN REPORTS GAINS
TOWARD BETTER DRUGS
THROUGH ISOSTERIC RE-
PLACEMENT, AT AAAS
CONFERENCE**

New Hampton, N. H.—Important new developments in the application of isosteric replacements to the development of new drugs and improvement of existing preparations were reported here at the Gordon Conference on Microbiological Deterioration of the American Association for the Advancement of Science, by Dr. H. L. Friedman, director of laboratory and technical research, Lakeside Laboratories of Milwaukee.

Isosteric replacements involve the

substitution of particular atoms or atom-groups for others, in such a way that the molecular three-dimensional shape is fundamentally unaltered. Dr. Friedman explained the theoretical implications of his work.

Practical results already achieved through isosteric replacements, he announced, include many commercial sulfonamides, antihistamines and antispasmodics.

Isosteric replacements might be called the "stand-ins" of the chemistry field, Dr. Friedman said. Shape is an important characteristic of any compound, as it is for any object. It may affect such properties as solubility of a compound. Even simple isosteric replacement may produce pronounced effects and provide a compound with more useful biochemical properties, Dr. Friedman said.

NEW ANTICHOLINERGIC IN GASTROINTESTINAL DISEASES

The effectiveness of diphenmethanil methylsulfate in the treatment of peptic ulcer and related gastrointestinal diseases has been demonstrated, according to Francesco D'Imperio in the *Journal of the Medical Society of New Jersey* 50:265 (June) 1953.

The 25 patients treated with this drug included 20 cases of peptic ulcer; two cases of diverticulum of the second portion of the duodenum, one of which also had a duodenal ulcer; two cases of hypertrophic gastritis, and two cases of esophageal achalasia, second and third degree.

The drug known as Prantal, relieved pain in 24 of these patients. In the one case where the drug was not efficacious, D'Imperio noted that a fair trial was not provided because of the unusual nature of the patient's past surgical experience and present symptomatology.

Five of the patients had been treated previously with another anticholinergic agent, which now failed to provide them with any relief. In all five of these cases Prantal was effective.

The dosage range varied from

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References:

1. Jankelson, I.R.: *Am. J. Digest. Dis.* 14:11 (Jan.) 1947
2. Flexner, J. (Discussion): *J.A.M.A.* 129:899 (Apr. 7) 1945
3. Metcalf, R.G.: *J. Maine M. A.* 44:183 (July) 1953

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1 cc. parenterally to 200 mg. orally every six hours. No side effects were observed. After disturbing symptoms were brought under control, the patients were maintained on a dosage that varied from 2 cc. parenterally to 200 mg. orally every six hours.

The author concluded that in Prantal a valuable drug for the treatment of peptic ulcer and related gastrointestinal diseases is available to the physician.

PARKE, DAVIS & CO. ESTABLISHES BRUSSELS BRANCH; FIRST COMPANY-OWNED FACILITIES IN EUROPE

Detroit.—Parke, Davis & Company has established a new branch office in Brussels, Belgium, W. R. Jeeves, vice president and direc-

tor of overseas operations, announced recently.

The pharmaceutical firm has major distributors in every European country outside the Iron Curtain, but the Brussels Branch is the first to be owned by the company on the Continent.

The branch occupies a three-story, recently-constructed building at 506 Chaussee de St. Job, approximately five miles south of the center of Brussels.

Jeeves said the new office will be under direction of the Parke-Davis London office, and L. R. Russell has been appointed manager. Dr. G. J. Pariser has been named field manager and E. Van Der Putten, chief accountant.

The new Brussels branch will serve approximately 8,400 physicians and 3,350 pharmacies in Belgium.

The building is of reinforced concrete with brick facing, 80 feet deep and with a 36 foot frontage, giving approximately 8,600 square feet of space. In addition to general offices, the building contains adequate warehouse space surfaced with semi-glazed small flagstones.

Jeeves explained that company representatives in Belgium must be especially trained, since the country is tri-lingual—French, Flemish and German.

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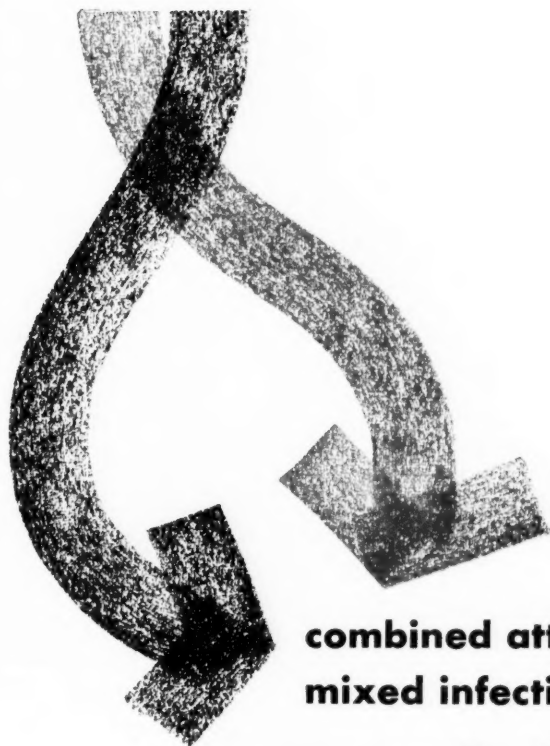
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University of California Medical School

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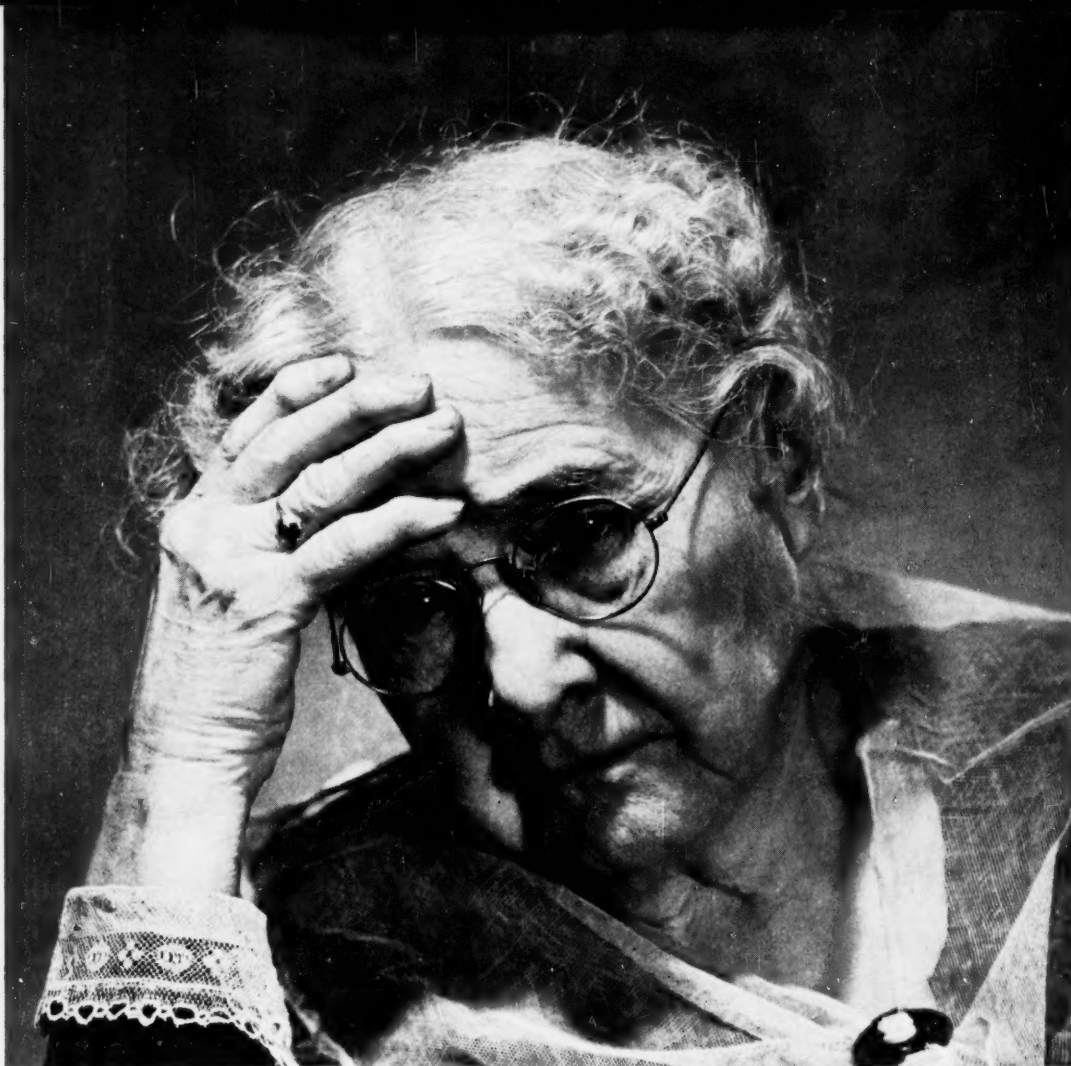
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